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EDITORIAL

LEARNING ENVIRONMENTS FOR UNDERGRADUATE MEDICAL STUDENTS

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Learning Environment for Medical Students is defined as everything that happens within the classroom, department, university, Teaching Hospital, or outside, that is essential in determining the success of undergraduate medical students. Learning environment for undergraduate medical students has two major areas: Medical College, and Teaching Hospital. Each one of them has many components. Each component has its own learning style, dynamics and rules to follow. Each learning environment provides students an opportunity to interact with peers and teachers, to have frequent feedback, to apply their learning in other situations, and to experience diversity. Classroom/Lecture Hall, Laboratory, Museums, Tutorial Room, College Auditorium, College Library, Play Grounds, Patient Bedside, Outpatient Department, Operation Theatre, Demonstration Room, Community Health Centre, MCH Centre, Vaccination Centre, and even the Examination Hall are all parts of learning environment of an undergraduate medical student.

Keywords: Learning environment, Medical students, Teaching Hospital, Medical College

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Learning environment refers to the diverse physical locations, contexts, and cultures in which students learn. Learning environment for medical students is defined as everything that happens within the classroom, department, university or teaching hospital or outside the medical institution that is essential in determining the success of undergraduate medical students.[1,2] The term also encompasses the culture of a school, its presiding ethos and characteristics, including how individuals interact with and treat one another, as well as the ways in which teachers may organize an educational setting to facilitate learning, e.g., by conducting classes in relevant natural ecosystems, grouping desks in specific ways, decorating the walls with learning materials, or utilizing audio, visual, and digital technologies.[2] An engaged learning environment increases students' attention and focus, promotes meaningful learning experiences, encourages higher levels of student performance, and motivates students to practice higher-level critical thinking skills.[3]

Learning environment for undergraduate medical students has two major areas, Medical College and Teaching Hospital. Each one of them has many components. Each component has its own learning style, dynamics and rules to follow. Each learning environment provides students an opportunity to interact with peers and teachers, to have their feedback, to apply their learning in other situations and to experience diversity.

Medical College:

In the medical college, there are many learning environments. The most well-known place in the medical college is Classroom or Lecture Hall which is meant for Large Group Teaching and Interactive Session. Rules to attend a classroom are very familiar to all of us as we are attending classroom from our childhood. Second very important place for learning is Departmental Laboratory. In Physiology, Biochemistry, Histology, Pharmacology, Pathology and Histopathology there are specified laboratories where students learn to develop manual skills and learn to use different medical equipment. Without an overall, students are not allowed to enter the laboratory. Students are required to learn how to handle human secretions which are potentially infectious and hazardous. There are museums in Anatomy, Pharmacology, Community Medicine and Forensic Medicine Departments where different types of learning materials are present. In Anatomy museum, models of different body parts and bones are displayed for the learning of the students. In Pharmacology museum, different drugs, medicinal herbs and instruments for preparation and dispensing of drugs are exhibited for students. In Pathology museum, diseased organs and body parts are present to show students the gross pathology of different diseases. There are tutorial rooms in the college for Small Group Discussion.

Library is an essential part of a medical college. It is a rich source of learning materials for students. It contains books on different medical subjects and specialties, medical journals, digital books and journals. High standard medical colleges have access to Higher Education Commission (HEC) Digital Library which is an excellent resource to access thousands of books and journals online. Attending the Library requires obeying its decorum like maintaining silence and switching off the mobile tone. There is a College Auditorium for Seminars, Conferences, Clinico-pathological conferences (CPC), Debates and convocation. As 'healthy mind lives in a healthy body',

there are Play Grounds in the college for indoor and outdoor games. They are also the learning environments for medical students. Apart from the Physical Fitness and exercise, students learn teamwork and undergo behaviour training, i.e., showing graceful and courteous behaviour while they win and show tolerance and undertake self-accountability when they lose.

Teaching Hospital:

In the teaching hospital, there are different wards for different clinical specialties in which relevant patients are admitted for indoor hospital care. This is a special learning environment that has its own dynamics and rules. Patients are the learning resource for the students but students should learn basic medical ethics and counselling/history taking skills before dealing with the patients. Not only patients are there but also physicians and nurses are the stakeholders with whom the students should learn to behave and interact. 'Bedside' is the best learning place for medical students to learn History taking, Physical Examination, Differential Diagnoses, Medical Investigations, Definitive Diagnosis, and Patient Management and Treatment. There are Demonstration Rooms in each ward where clinical cases of that specialty are presented to the students and history taking, physical examination and diagnostic process are discussed with the students.

Out-Patient Department is another very important place in the teaching hospital where medical students learn different aspects of ambulatory care. Students take history, perform physical examination and prepare case for discussion with their medical teacher for learning.

Operation Theatre is a special learning environment for medical students. Here the students are required to wear masks, cover their heads with a cap and wear aseptic clothing or overall before entering the operation theatre. They are told not to touch any object in the theatre with their hands.

Vaccination Centre is also present in the teaching hospital. Students visit this centre to learn about the vaccination program being run in the country and they learn different aspects of Preventive Medicine.

Community Health Centre and MCH Centre are also the learning environments for medical students which are located away from their teaching institution. Medical students visit Community Health Centre (Basic Health Unit or Rural Health Centre) during their Community Medicine tour program to be familiar with the Health Delivery System practiced in the country. In Pakistan, Maternal Mortality Rate (MMR) and Under 5 Mortality Rate are still higher, and Mother and Child Health is top priority program. MCH Centre tour is a well focused component in Community Medicine.

Examinations are very important learning opportunities for the students. Examination hall has very different environment than the normal learning environments. In the examination hall, students learn Time Management when they allocate time for answering the questions. They also learn to use the precise writing skill when answering an extensive question in a short time. They also learn to use explanation skill in answering a question when answering material is short and the time is sufficient. During viva voce examination, students learn Communication Skill and to work under stress. During OSPE and OSCE students learn and practice patient dealing skills.

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ORIGINAL ARTICLE
MEVASTATIN: A NOVEL AGENT FORMING DOPAMINERGIC NEURONS FROM HUMAN MESENCHYMAL STEM CELLS

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Background: Human umbilical cord derived mesenchymal stem cell (hUMSCs) are in experimental phase for treatment of various neurological disorders. Differentiating these cells into neurons is expensive and painstaking. Mevastatin a commonly used antihyperlipidemic agent is known for its neuroprotective effect. We investigated the differentiation response of human umbilical cord derived mesenchymal stem cell (hUMSCs) to Mevastatin. **Methods:** In this dose-response experimental study, hUMSCs were isolated and characterized for presence of specific stem cells markers (cd90, cd73, cd105, oct4) by conventional PCR and Immunocytochemistry (Vimentin, cd24, cd90). Then, the cytotoxicity of the compound (Mevastatin) was analyzed to select the best working concentration for neuronal differentiation. Cells were grown in the presence of the least cytotoxic concentration for 2 weeks. The differentiated cells were analyzed for morphological changes and neuron specific markers by qPCR and Immunocytochemistry. **Results:** hUMSCs derived dopaminergic neurons to be similar to those found in the human midbrain based on cell type and results showed positive expression of dopaminergic neuron specific genes (TH, NURR1, LMAX1). Positive expression of TH was observed in the differentiated cells. Additionally, the differentiated cells lost the expression of stem cells specific marker cd24, which was evident in the control cells. **Conclusion:** Mevastatin can differentiate hUMSCs into dopaminergic neuron like cells at 1 µM concentration. Using Mevastatin (when required) in those dyslipidemic patients who have increased susceptibility to Parkinson's disease is suggested. However, further research in this direction is recommended.
Keywords: Cell-therapy in Parkinsonism, Neurodifferentiation by Mevastatin, Dopaminergic neuron formation

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative progressive disorder affecting millions of people worldwide. It is characterized by typical movement disorder including rigidity, tremors and bradykinesia.[1] It is identified pathogenically by, the presence of Lewy bodies made up of misfolded α-syn[2] protein.[2]

Current treatments of Parkinson's disease (PD) include levodopa, monoamine oxidase type B (MAOB) inhibitors, and catechol-o-methyl-transferases (COMT) that help in improving few symptoms of the disease. However, with continuous use patients develop drug resistance and eventually other modalities need to be used. A common such method is deep brain stimulation (DBS). This has limited benefit in reduction of symptoms and can be used only in some specific patients.[3]

In PD Gene therapy has been considered as hopeful treatment approach. The aim of gene therapy is to modify the expression of neurons in basal ganglia that have degenerated with resultant decreased release of dopamine.[4] Genetic modifications are in the experimental phase and require extensive testing before these can be introduced in humans.[5,6]

Cell-based therapies have attracted attention of the researchers as being potentially feasible for neurodegenerative diseases. It encompasses derivation of specific neuronal cells and consequent transplantation into affected parts of the neuronal system. Different cell types have been used for differentiation of dopaminergic neurons and subsequent transplantation into patients with PD.[7] These include embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs) etc. ESCs have a potential to differentiate into 3 three primary germ layers. However, their use is restricted due to ethical issues and high risk of teratoma formation after transplantation.[8] iPSCs on the other hand are very important tools for drug development, regenerative medicine and diseases modelling. Furthermore, they are considered superior to ESCs as a cell source for PD replacement, including the capability to use patient's peculiar cells and consequently reduce the necessity for immuno-suppression. However, their

use could be limited due to their high risk of teratoma formation after transplantation.[8]

Adult stem cells are obtained from all tissues of the three germ layers, for example MSCs can be derived from human amnion epithelial cells. They are easy to separate, have more differentiation potential with fewer ethical problems.[9,10] MSCs release the soluble factors that are significant for cell existence and proliferation.[11] Different small molecules have been used to differentiate hUMSCs into neurons. These include Valproic acid fibroblast growth factor and Forskolin.[12] It was observed that statin molecules are effective in both neuronal differentiation and mid brain neuron specification.[12] Various statin molecules have been implicated to cause similar differentiation, however Mevastatin has been shown to be superior in this effect to others.[13]

This study was designed to investigate the differentiation potential hUMSCs into dopaminergic neurons using Mevastatin.

METHODOLOGY

This was a dose response in-vitro experimental study carried out at Ziauddin University from August 2019 to February 2020 after approval from the Ethics Review Committee of Ziauddin University.

Umbilical cords were obtained from babies of primigravida mothers between 18 to 30 years of age with no known comorbid and pregnancy related complications.

The cord was washed numerous times with purified PBS solution and cut into 3 mm thick parts. Cord tissues were minced with scissors and processed with Trypsin 10X act as digest. The isolated cells there were plated in DMEM (Life Technologies) supplemented with 10% foetal bovine serum (FBS), and 100 mg/mL streptomycin 50 mg/mL penicillin (Life Technologies) at 37 ℃ in a moistened 5% CO_2 incubator.

RNA was isolated from control hUMSCs with Trizol reagent according to the optimized protocol. The isolated RNA was stored in nucleus free water (Life Technologies) at -80 ℃.

RNA was quantified by using multi scan skey spectrophotometer and the kit revert aid first stand cDNA synthesis kit (M/S Thermo Scientific) was used for one microgram RNA reverse transcription according to manufacturer's protocol.

The cDNA was either used directly for PCR or kept at -20 ℃ till further usage.

For Primer designing we used the primer3 design program at http://frodo.wi.mit.edu/primer3/, and bought from Pericon.

q-PCR of hUMSCs cells were used for the expression of stem cells markers (CD73, CD 105, CD 133, Oct-4) GAPDH was used as an internal standard.

Then PCR products were evaluated by gel electrophoresis. The Gel documentation system was used to study the gel.

hUMSCs cells (~10,000 cells) were cultured in 24 well plates, processed according to standard protocol and viewed using an inverted fluorescent microscope.

hUMSCs were treated with different concentration such as (1 µM, 5 µM, 10 µM, 50 µM, 100 µM) of Mevastatin and morphology of the cells was observed at different times intervals 24, 48, and 72 hours with performing the following steps.

To evaluate cytotoxicity in cells after treatment with different concentrations of Mevastatin, trypan blue exclusion (Life Technologies) procedure was performed. Cells were cultured in 24-well plate and incubated with different concentrations of Mevastatin (1 µM, 5 µM, 10 µM, 50 µM and, 100 µM)[12] cytotoxicity was observed at different time interval.

Live and dead cells were counted separately to calculate the cytotoxicity according to the formula:

$$\text{Viable cells (\%)} = \frac{\text{Total No. of viable cells/mL of aliquot}}{\text{Total No. of cells/mL of aliquot}} \times 100$$

When live cells reached 70% to 80% of confluency, by using 1 µM least cytotoxic concentration of Mevastatin was used for the differentiation induction of hUMSCs and media was replaced after each 3rd day followed by morphological and gene expression analysis of the differentiated cells after 2 weeks.

All the groups were analysed for morphological changes by Floid Cell Imaging System and compared with untreated control and images were captured at 40× magnification.

The treated cells RNA was isolated by using Trizol and Revert Aid cDNA synthesis Kit was used for reverse transcription of RNA. Expression of neuron specific markers (TH, NURR1 and LMXa1) were examined by real time-PCR. Following completion of 40 cycles, CT values were acquired and used to determine the result of relative fold chain using the formula:

$$\Delta Ct = Ct\ (Gene) - Ct\ (GAPDH)$$
$$\Delta\Delta Ct = \Delta Ct\ (Sample) - \Delta Ct\ (Control)$$
$$\text{Fold change} = 2^{-(\Delta\Delta Ct)}$$

Differentiated cells (~10,000 cells) were cultured in 24 well plates by adding 1 mL of cell suspension (1× cells). The cells were labelled against primary antibody TH, LMXIA, NURR1 and

CD24 was used as stem cell marker, further procedure had been processed according to standard protocol and viewed using an inverted fluorescent microscope.

Statistical analysis was carried out using SPSS-20. Quantitative variables were calculated as percentages. Student's t-test was carried out as a measure of difference and a $p<0.05$ was considered significant.

RESULTS

After propagation, characterization of hUMSCs was done by morphological examination, gene expression analysis (OCT 4, CD105, CD73) using GAPDH gene as internal standard and protein expression analysis (Actin, Vimentin, CD24).

The hUMSCs were then treated with different concentrations of Mevastatin (1, 5, 10, 50 and 100 μM). The cells were analyzed in the following steps:

No cytotoxicity was observed at the concentration of 1 μM at 72 hours. However, we found that cells showed high cytotoxicity and cell death along with no differentiation (neuron morphology) under our observation at 5 μM, 10 μM, 50 μM, 100 μM at 24 and 48 hours respectively. (Figure-1).

Cytotoxicity was calculated using the formula which was mention above. Our results showed that the cell viability at 1 μM was around 93.89% which was highest when compared to other concentration.

Morphological examination of differentiated hUMSCs was carried out 2 weeks after treatment with Mevastatin using inverted microscopy. Dopaminergic-neuron-like cells were found after treatment with 1 μM concentration of Mevastatin at 72 hours. Cells showed multipolar shaped neuron formation. Hence 1 μM concentration of Mevastatin was considered as least cytotoxic and used for differentiation induction. (Figure-2).

Genes expression analysis of differentiated specific genes such as TH, NURR1, LMXIA were determined by using q-PCR. GAPDH was taken as positive control. Our results showed that expressions were significantly increased ($p<0.05$) after 1 μM Mevastatin treatment as compared to control. (Figure-3).

Basal level of Actin, CD24, and TH proteins were analysed in the treated cells by direct immunofluorescence. The cells of control and treated showed positive expression of actin while CD 24 negative expression in treated cells, Tyrosine protein highly expressed in treated cells. (Figure-4).
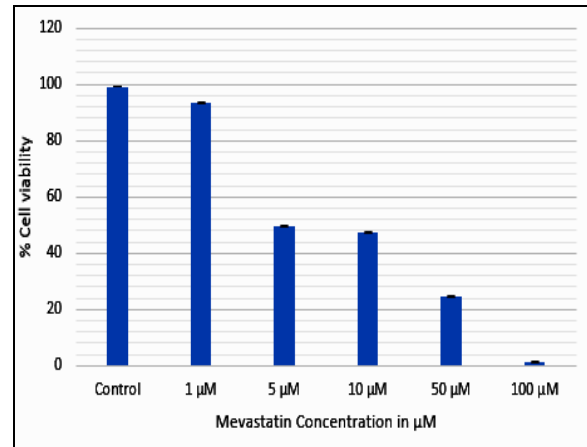
Figure-1: Cell viability after treatment with Mevastatin
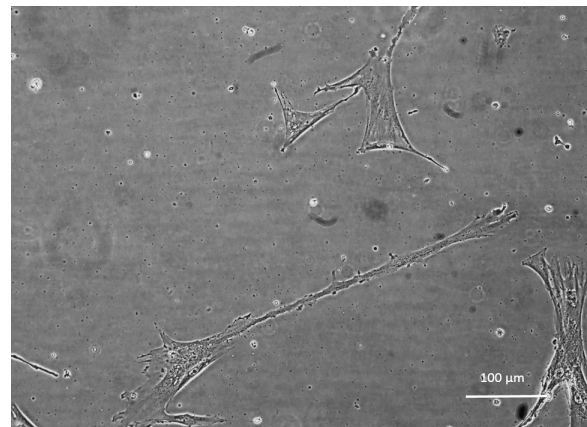
Figure-2: Differentiated hUMSCs were observed dopaminergic neuron like cells after the treatment of 1 μM concentration of Mevastatin at 72 hours after 2 week. Cell showed multipolar in shaped, analyzed under inverted microscopy at 10× magnification.
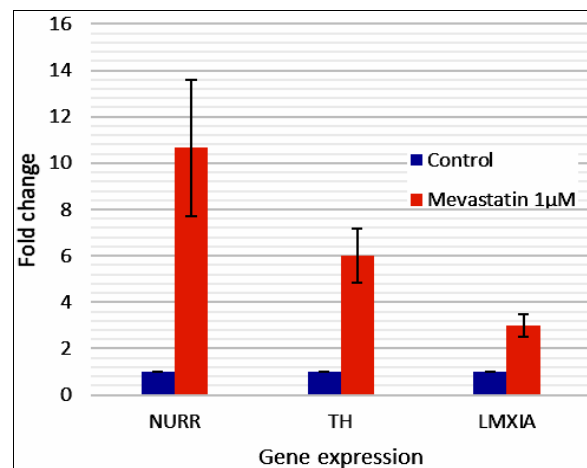
Figure-3: Expression of neuron specific genes by qPCR

Combined graphical presentation of all genes expression were significantly increased ($p<0.05$) in the Mevastatin treatment groups compared to control
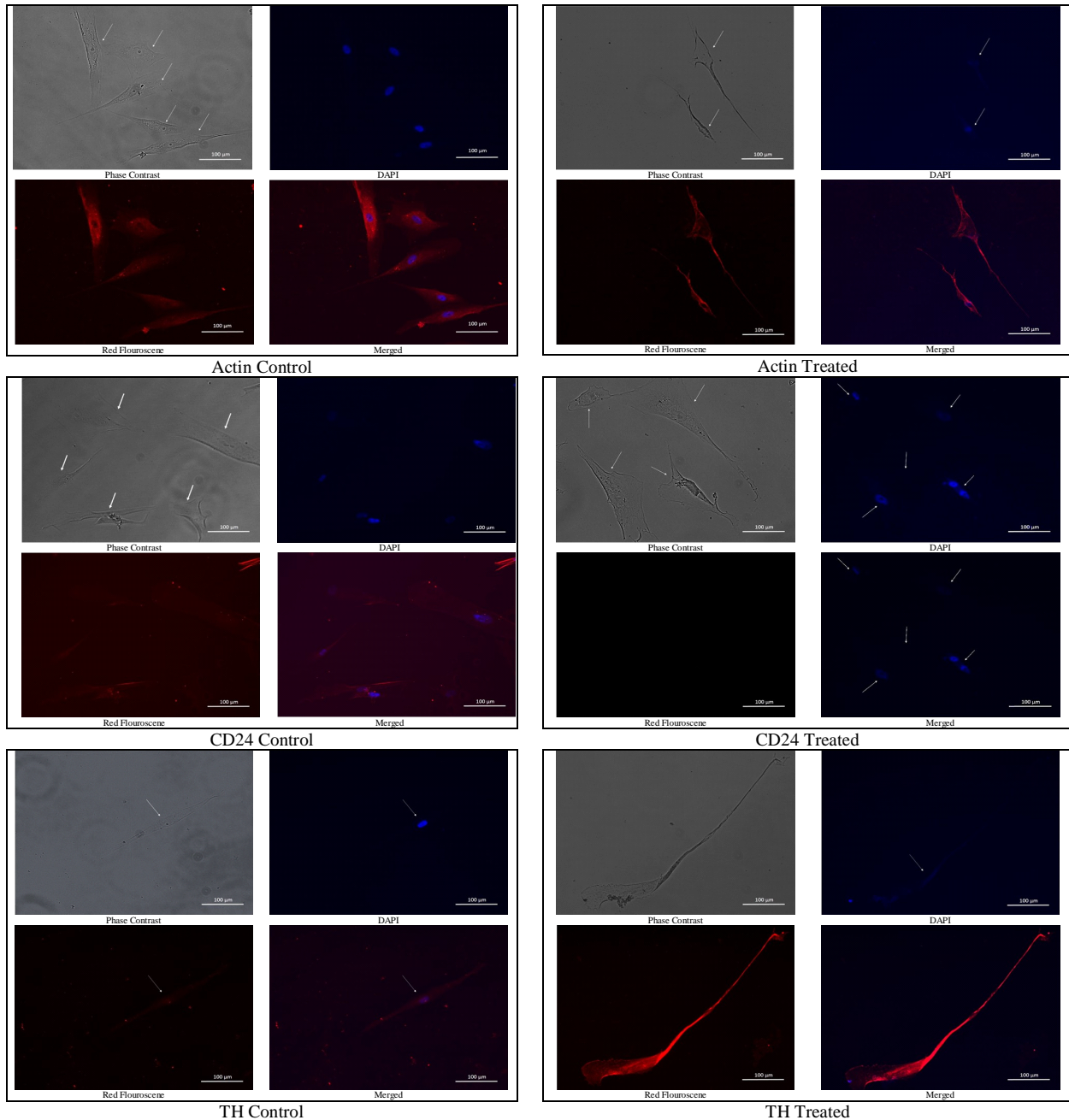
Figure-4: Immunocytochemical analysis of differentiated human umbilical cord derived mesenchymal stem cells
Actin showed positive in control and treated cells with neurogenic changes. The cells showed high expression of CD24 in the control and no expression in the treated cells. The Tyrosine protein showed low expression in the control whereas the Tyrosine protein showed highly expressed in the treated cells and exhibited dopaminergic neuron differentiation. Alexa fluor 546 anti-rabbit antibody was used for recognition. DAPI was used as stained in Nuclei. $100\times$ magnification on Florid microscope.

DISCUSSION

The field of cell therapy and regenerative medicine holds great promise in restoring normal tissues structure and function. The main aim of stem cell based therapies is to target the chronic diseases and lifelong disabilities.[14] The best example of stem cell is MSCs, which have ability to differentiate into neuron-like cells and release different chemokines and growth factors.

These growth factors and chemokines are necessary in revascularization, neurogenesis, immunomodulatory, anti-apoptotic and anti-inflammatory effects and have ability to engraft and migrate at sites of injury and inflammation.[15]

We have attempted to differentiate hUMSCs into neurons using Mevastatin, a commonly used antihyperlipidemic agent[16]. Mevastatin has potential to direct differentiate the neural progenitor cells into

dopaminergic neurons for the Parkinson's diseases.[12] These cells have been reported to have increased expression in proliferating hUMSCs previously.[17,18] In addition, we also checked for increased expression of the proteins Actin, Vimentin and CD24. These protein markers, especially Vimentin, were shown in multiple studies to be strongly positive.[17,19] They are also expressed in α-smooth muscle actin.[19]

At Mevastatin 1 μM concentration, characteristic properties of dopaminergic neurons in these cells, such as multipolar, unipolar and bipolar differentiation, star and diamond shaped cells, as well as elongated axon and/or dendrites were observed. These observations were validated in accordance with previous studies[20,21]. After confirmation of morphology, dopaminergic differentiation was further validated by demonstrating increased expression of NURR1, LMXIA and TH genes. These genes have been used demonstrating conversion of neuroprogenitor cells into dopaminergic neurons by using LY364947 and Mevastatin.[12]

Immunocytochemistry showed that the differentiated hUMSCs were positive for TH and Actin as well. However, a negative expression of CD24 was observed. These finding are in accordance with a similar experiment carried out on Wharton's Jelly derived mesenchymal stem cells differentiating into neuron-like cells using 1 mM concentration of Valproic acid.[22]

CONCLUSION

Mevastatin can differentiate hUMSCs into dopaminergic neuron like cells at 1 μM concentration. Using Mevastatin (when required) in those dyslipidemic patients who have increased susceptibility to Parkinson's disease is suggested. However, further research in this direction is recommended.

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Contribution of Authors:
HA: Original idea, sample collection and initial writing
SU: Sample processing and results, experimentation
STA: Proofreading and critical analysis
KH: Referencing, literature review and sample processing
SH: Data analysis, grammar and article writing and final detailing
KJJB: Inference, critical analysis and logical reasoning

ORIGINAL ARTICLE
COMPARATIVE EFFECT OF ALPHA TOCOPHEROL AND ASCORBIC ACID ON BODY WEIGHT OF RATS EXPOSED TO CHRONIC RESTRAINT STRESS

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Background: The stress is defined as the constellation of events, which begins with a stimulus, and subsequently results in the activation of certain physiologic systems. This study was planned to determine the comparative effect of ascorbic acid and alpha tocopherol on body weight of Sprague Dawley rats exposed to chronic restraint stress. **Methods:** This comparative experimental study was done in National Institute of Health (NIH), Islamabad. One-hundred-and-twenty male Sprague Dawley rats (mean weight 250±50 grams) were used and divided into 4 equal groups. Group I was taken as control. Group II was exposed to chronic stress, Group III was given only ascorbic acid prior to restraint stress, and Group IV was given only alpha tocopherol prior to restraint stress. Group III & IV were given prior supplementation of ascorbic acid, alpha tocopherol for 1 month. **Results:** There was a significant decrease in weight gain of rats exposed to the chronic stress as compared to control group. Individual supplementation with ascorbic acid and alpha tocopherol resulted in significant improvement of their eating habits with rats supplemented with ascorbic acid. **Conclusion:** Chronic stress has a detrimental effect on weight. This effect can be minimised by the intake of sufficient amount of antioxidants.
Keywords: Ascorbic acid, alpha tocopherol, body weight, chronic stress, cortisol, antioxidant

INTRODUCTION

Stress is known to change body weight and food intake in animal models. Stress is a widespread problem of today's life where stressors are increasingly prevalent.[1] Best way to prevent stress in life is to adopt a healthy lifestyle which includes good nutrition, moderate exercise, sufficient sleep, meaningful work.[2] Stress is commonly known to change body weight and food intake in animals. Of the various stress models available for the study of the effects of stress, the restraint stress model is most commonly used, as it effectively expresses physical and psychological stress.[3] The restraint stress technique has also been used as an animal model of depression. Many studies have shown that restraint stress decreases food intake and body weight gain in rats.[4,5] The central regulation of body weight and food intake occurs in the hypothalamus, which encompasses multiple neuronal systems, that play important roles in the regulation of energy homeostasis.[6] The weight loss due to stress is dependent on the acute central release of corticotrophin-releasing factor (CRF)[7], but there is no continuous activation of this pathway to determine for the maintained suppression of body weight.[8,9] The CRF activates hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic nervous system, and catecholamine systems. All of these mechanisms likely to inhibit food intake and reduce body weight, but none of them is activated notably during the hours or days after exposure to repeated restraint. Moreover, the defensive role of antioxidant in reducing weight loss is still unclear. Several studies have acknowledged the valuable effects of ascorbic acid supplementation on stress induced changes.

Keeping in view the beneficial role of antioxidants, this study was designed to determine the role of individual supplementation of ascorbic acid and alpha tocopherol in preventing the deterioration in body weight due to chronic restraint stress.

MATERIAL AND METHODS

Total 120 Sprague Dawley healthy male rats weighing 250±50 grams, 60 days (8 weeks) old were obtained from National Institute of Health (NIH), Islamabad. Females, diseased, or those rats developing any disease during the course were excluded from the study. Rats were divided into 4 equal groups. Group-I was considered as control group. Rats in this group were fed with normal diet without any supplementation. They were supplied simple tap water for drinking. Rats in Group-II were given standard diet without any supplementations, and were exposed to daily stress for 15 days. Rats of Group III were supplemented with ascorbic acid in a dose of 500 mg/l added in drinking water and Group IV were supplemented with alpha tocopherol 300 mg/l supplement with Soya bean oil for one month before and during chronic stress. All animals were kept in a separate cage compartments to monitor intake of diet.

Rats of group II, III and IV were exposed to chronic stress by keeping immobilized in a mesh wire restrainer for 6 hours daily for 15 days.[9,10] Stress was determined by serum cortisol level. Samples were taken

early in the morning between 8 and 9 AM, to avoid bias due to different levels of cortisol owing to the diurnal variations.[11]

Composition of pelleted diet for rats was as under:

> Wheat flour 2.85 Kg, Wheat brawn 2.85 Kg, Dried skimmed milk powder 2.0 Kg, Soya bean oil 0.5 Kg, Mollasen 0.15 Kg, Fish meat 0.15 Kg, and Table salt 0.05 Kg

This food was prepared at (NIH), Islamabad, according to the standard approved by the Universities Federation for Animals Welfare. Eating habits and behavioural changes were also observed throughout the duration of the study.

For statistical analysis SPSS-15 was used. Mean and standard deviation of body weight were calculated. The statistical significance of difference across the groups was determined by applying ANOVA followed by Post Hoc Test to find difference in various pair of groups. The difference was considered significant if $p<0.005$

RESULTS

The rats remained healthy and active throughout the study. The average intake of feed by each rat was between 15–20 grams. If the rats took more than 20 grams of diet per day, it will be considered 'improved' while less than 15 grams' intake was considered 'reduced' (Table-1). Average weight of all rats at the start was 220 grams.

The comparison of weight gains by the different groups (Table-2) showed that there was a significant decrease in weight gain of rats exposed to chronic stress as compared to control group.

Nevertheless, individual supplementation with ascorbic acid resulted in significant improvement of their eating habits as comparted to alpha tocopherol supplementation. (Table-3). Serum cortisol level when compared among different groups was the highest in group II indicating high levels of stress in that group. (Table-4).

Table-1: Comparison of body weight in different study groups of Sprague Dawley rats (gm, Mean±SD)

Weeks	Control (n=30)	Stress (n=30)	Ascorbic (n=30)	Tocopherol (n=30)	p
9th	235.17±7.48	234.17±7.32	244.67±7.18	238.33±5.31	<0.001
10th	261.00±6.07	261.67±7.11	282.50±5.37	271.50±6.18	<0.001
11th	279.33±6.26	279.33±7.63	299.00±6.49	291.33±6.94	<0.001
12th	300.00±5.72	299.50±7.70	320.00±6.70	303.33±7.35	<0.001
13th	313.83±6.78	306.83±7.13	330.17±6.09	328.50±11.61	<0.001
14th	320.17±6.83	309.50±7.58	362.50±6.99	305.83±33.43	<0.001

Table-2: Comparison of body weight of the groups during different weeks using Post-Hoc (Tukey) test (*p*=value)

Group Comparison	9th week	10th week	11th week	12th week	13th week	14th week
Group I and II	0.981	0.994	1.000	0.999	0.001	<0.001
Group I and III	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Group I and IV	0.389	<0.001	<0.001	0.328	0.040	<0.001
Group II and III	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Group II and IV	0.144	<0.001	<0.001	0.196	<0.001	<0.001
Group III and IV	0.005	<0.001	<0.001	<0.001	<0.001	<0.001

Table-3: Comparison of eating habits of rats in different groups

Groups (n=30)	9th week	10th week	11th week	12th week	13th week	14th week
Control	Normal	Normal	Normal	Normal	Normal	Normal
Stress	Normal	Normal	Normal	Normal	**Reduced**	**Reduced**
Ascorbic	Normal	**Improved**	**Improved**	**Improved**	Normal	Normal
Tocopherol	Normal	Normal	Normal	Normal	Normal	**Improved**

Normal: daily dietary grams; Reduced= dietary intake less than 15 grams/day; Improved= dietary intake >20 intake of each rat= 15–20 grams/day.

Table-4: Serum cortisol levels in study groups (Mean±SD)

Variable	Group I	Group II	Group III	Group IV	p
Cortisol	21.4±0.92	34.71±1.45	30.31±0.81 ng/ml	32.23±1.22 ng/ml	<0.001

Table-5: Statistical differences of serum cortisol between different groups using Post-Hoc (Tukey) test

Comparisons	p
Control and Stress	<0.001
Control and ascorbic	<0.001
Control and tocopherol	<0.001
Stress and ascorbic	<0.001
Stress and tocopherol	<0.001
Ascorbic and tocopherol	<0.001

DISCUSSION

In the present study, we examined the effects of separate supplementation of ascorbic acid and alpha tocopherol separately on the body weight and food intake of Sprague Dawley rats exposed to chronic restraint stress. Several studies have tried to establish the fact that chronic exposure to restraint stress reduces the body weight and food intake of rats.[12–14] However, the mechanisms underlying these restraint-induced fluctuations in body weight and food intake remain to be elucidated. Our results have shown that restraint stress speedily induce a marked reduction in body weight that may be due to a decreased food intake. The stress-induced decrease in body weight may be due originally to an early decrease in food intake but then may be subsequently maintained by increases in energy expenditure and body temperature during restraint. Increased serum cortisol levels suggest that physiological responses to repeated stress are associated with the stimulation of the HPA axis. Results of study

conducted by Santos *et al*[14] back our results that chronic stress causes reduction in weight gain (2.0±0.65 g/day), while Dallman *et al*[15] have documented differing results and hypothesized that chronic stress resulted in increase in weight gain (2.5±0.32 g/day). It might be due to reduction in growth hormone secretion, reduced linear growth, and sympathetic neural outflow along with reduced fat mobilization, which led to obesity.[15] This study also showed that, during exposure to restraint stress significantly decreased food intake, once the stress ended, the food intake of the stressed group returned to the normal level. Serum corticosterone levels were increased by repeated restraint stress. Effect of separate supplementation with ascorbic acid and alpha tocopherol has been documented by different studies as more potent as compared to study by Engel *et al*[16] who documented that separate use of ascorbic acid and alpha tocopherol enhanced not only the immune status by decreasing serum cortisol level but also the body weight.

The data of present study has disclosed that stress; whether psychological or physical could lead to lower the immune status of the individual. Stress is one of the important factors, which, in one way or the other, disrupts many physiological functions. Higher the intensity or duration of stress, greater will be the disruption. The use of antioxidants supplements can be one of the means by which we can prophylactically protect our body from the harmful effects of stress.

CONCLUSION

Chronic restraint stress is responsible for elevated serum cortisol level which directly or indirectly affects the food intake, and reduces the body weight. However, those animals on prior supplementation of ascorbic acid showed much improvement in food intake and weight gain as compared to alpha tocopherol supplementation.

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Contribution of Authors:
SM: Design research, data collection and analysis, manuscript writing
FM: Sample collection
RS: Sample collection
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ORIGINAL ARTICLE

VISFATIN AS A BIOMARKER FOR EARLY DETECTION OF GESTATIONAL DIABETES MELLITUS

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Background: The increased levels of visfatin in response to slowly developing resistance to insulin and impairment of glucose metabolism in human body is a well-documented process, beginning early in with uncontrolled diabetes and obesity The objective of present study was to determine the difference between levels of visfatin in the gestational diabetes mellitus cases and pregnancies with normal OGTT. **Methods:** It was a case control study conducted in Ayub Teaching Hospital Abbottabad. Twenty-eight (n=28) diagnosed cases of gestational diabetes mellitus at various gestational ages (ranging from 11 weeks to 33weeks of pregnancy) were included in the Group I and their levels were compared with non-diabetic normal antenatal cases, Group II (n=32). Blood samples were collected for blood glucose and visfatin levels. Visfatin levels were measured by enzyme-linked immunosorbent assay (ELIZA). Statistical analysis was performed on SPSS-20, and $p<0.05$ was taken as significant. **Results:** Pregnant women (n=60) of different gestational age ranging from 4–36 weeks of pregnancy when subdivided into three categories (4–12 weeks, 13–24 weeks, 24–36 weeks respectively), showed statistically significant ($p=0.003$) differences of serum visfatin levels (10.11 ± 2.982, 1.01 ± 2.634, 1.17 ± 3.102 ng/ml respectively). There were no significant differences in mean value of serum visfatin ($p=0.763$) according to parity of the patients (0.16 ± 2.892, 0.19 ± 2.883, 1.01 ± 2.736 respectively) in the three trimesters of pregnancy. **Conclusion:** Visfatin levels were significantly raised in gestational diabetes mellitus as early as first trimester of pregnancy. Increased levels of visfatin can be used as a novel biomarker for early detection of gestational diabetes mellitus.
Keywords: Visfatin, insulin resistance, gestational diabetes mellitus

INTRODUCTION

Various adipokines like resistin, adiponectin, IL-6, leptin, TNF and visfatin play quite significant roles in regulation of glucose, lipids and energy metabolism leading to the development of abnormal cascade of metabolism in cardiovascular, reproductive immune system.[1] Due to unique mechanism of action of visfatin on insulin resistance it initiates the cascade of intracellular signalling of insulin like stimulation of phosphorylation of tyrosine kinase and activation of protein kinase B but in different manner than insulin itself leading to development of Gestational Diabetes Mellitus (GDM).[1,2]

Visfatin has been implicated in many disease entities including atherosclerosis, obesity due to visceral fat mass[3], type II diabetes mellitus[4], renal and, beta cell functional impairment and metabolic syndrome[3,4] and tumour replication[5]. During pregnancy the level of visfatin which is complicated by glucose intolerance may sometimes be increased or decreased.[1]

GDM is the glucose intolerance which is diagnosed for the first time during pregnancy.[6] Visfatin is found to be produced by adipocytes, placental tissues and the membranes of the fetus.[7] Some international studies suggest that there is significant increase in visfatin levels in pregnancies with GDM compared to the controls suggest that there might be a role of this peptide in the worsening of insulin resistance in normal pregnancies ultimately progressing to gestational diabetes mellitus.[8]

The finding of increased serum levels of visfatin at early pregnancy (11–13 weeks) in pregnant women is a new one, who subsequently develop GDM in later pregnancy.[7] There is evidence that, in pregnancy, the source of circulating visfatin is not only visceral fat, but also the placenta and the increased serum concentration observed in GDM may be the consequence of placental over-secretion.[9]

Visfatin may have a role in development of gestational diabetes and can worsen the consequences if not detected and treated earlier. With timely risk factors manipulation and intervention, the worsening of disease and development of maternal and foetal complications could be avoided. This study aimed to see the difference between levels of visfatin in the gestational diabetes mellitus cases and pregnancies with normal OGTT.

MATERIAL AND METHODS

This was an observational cross-sectional study. We sought to determine the levels of maternal serum visfatin in pregnancy as a biomarker for the detection of uncontrolled diabetes mellitus (gestational diabetes mellitus GDM). Written informed consent was taken from women who agreed to participate in the study.

Sampling was done through technique of convenience sampling.

Pregnant women (60) of different parity and gestational age were divided into two groups. Twenty-eight diagnosed cases of gestational diabetes mellitus at various gestational ages (11–33 weeks) were included in Group I and their levels were compared with non-diabetic normal antenatal cases, Group II (controls, n=32). Weight (Kg), height (m), and body mass index (BMI) (Kg/m^2) were recorded. Subjects were divided into four sub-groups according to their BMI. Normal weight (18.5–22.9), underweight (<18.5), overweight (23–24.4) and obese (>25). BMI was classified according to the static requirements for Asian population.[10]

Blood pressure, and period of gestation were recorded as their routine antenatal examination, and previous or family history of gestational diabetes was taken. The fasting blood samples were collected through venepuncture for levels of blood glucose and serum visfatin. Women were categorized into two groups (cases and controls) with blood glucose levels >6.75 mmol/L suspected for gestational diabetes with positive family or previous history of DM. In order to confirm the diagnosis of GDM an oral glucose tolerance test was performed by giving 75 gm oral glucose and measurement of plasma glucose level after two hours. Levels more than 7.8 mmol/L were taken as confirmed cases of GDM.[11] The cases and controls were further analyzed for serum visfatin levels. Maternal serum visfatin concentration was measured quantitatively by ELISA technique using eNampt/PBEF ELISA kit for visfatin of Alpco Diagnostics.

Statistical data analysis was performed on SPSS-20. For continuous variables like serum visfatin, Mean±SD was calculated and for categorical variables like BMI, period of gestation, and parity, frequencies and percentages were calculated. Two-way Student's *t*-test was applied for comparison of serum visfatin in various sub-groups of pregnant women, and *p*<0.05 was taken as statistically significant.

RESULTS

The mean age of women in our study group was 32.8 (26.4–39.2) in years. Weight and height of all patients were recorded to calculate BMI; 35 (58.33%) women were of normal weight, 2 (3.33%) were under weight, 15 (25%) were overweight and 8 (13.33%) were obese. There were statistically significant differences (*p*=0.001) among four subgroups of women according to their BMI (1.06±0.025, 1.05±0.031, 3.53±0.094, 3.92±0.193). Pregnant women (n=60) of different gestational age ranging from 4–36 weeks of pregnancy when subdivided into 3 categories (4–12 weeks, 13–24 weeks, 24–36 weeks respectively), showed statistically significant (*p*=0.003) differences of serum visfatin levels

(10.11±2.982, 1.01±2.634, 1.17±3.102 ng/ml respectively). Among all pregnant cases 12 (20%) were primipara, 22 (36.66%) were multigravida, and 26 (43.33%) were grand multigravidas with more than five pregnancies. There were no significant differences in mean value of serum visfatin (*p*=0.763) according to parity of the patients (0.16±2.892, 0.19±2.883, 1.01±2.736 respectively) in the three trimesters of pregnancy. In our study 32 (53.33%) were non-diabetic, and 28 (46.66%) were cases of gestational diabetes having significant (*p*=0.0001) differences in mean serum visfatin levels (1.06±0.013 and 3.82±0.193) (Table-1).

Trimester-wise stratification of study population into diabetic and non-diabetic (cases and controls) showed high percentage of impaired glucose tolerance in pregnant women in 1st trimester (61.53%) and 2nd (35.7%), and 3rd trimester (52.63%) respectively (Table-2).

The differences of mean values of serum visfatin, blood glucose and glycosylated haemoglobin between group I and II and their statistical significance (*p*=0.0001) in each case showing the positive correlation between gestational diabetes and visfatin metabolism are tabulated as Table–3.

Table-1: Pregnancy variables and descriptive characteristics of subjects

Parameter	n (%)	Serum visfatin (ng/ml)	*p*
BMI (Kg/m^2)			
Normal (18.5–22.9)	35 (58.33)	1.06±0.025	
Underweight (<18.5)	2 (3.33)	1.05±0.031	0.001
Overweight (23–24.4)	15 (25)	3.53±0.094	
Obese (>25)	8 (13.33)	3.92±0.193	
Period of Gestation			
4–12 weeks	13 (21.66)	0.11±2.982	
13–24 weeks	28 (46.66)	1.01±2.634	0.003
24–36 weeks	19 (31.66)	1.17±3.102	
Parity			
Primipara (1st)	12 (20)	0.16±2.892	
Multigravida (2–4)	22 (36.66)	0.19±2.883	0.763
Grand multigravida (≥5)	26 (43.33)	1.01±2.736	
Diabetic status			
Non-Diabetic	32 (53.33%)	1.06±0.013	0.0001
GDM	28 (46.66%)	3.82±0.193	

Table-2: Trimester-wise stratification of study population into two groups (cases and controls)

GROUPS	Trimester		
	I (4–12 weeks)	II (13–24 weeks)	III (25–36 weeks)
GDM	8 (61.53%)	10 (35.7%)	10 (52.63%)
Non Diabetic	5 (38.46%)	18 (64.28%)	9 (47.37%)

Table-3: Differences between serum visfatin, plasma glucose level, and glycosylated haemoglobin in two groups (Mean±SD)

Variable	Groups I (Cases)	Group II (Controls)	*p*
Serum visfatin (ng/ml)	3.82±0.193	1.06±0.013	<0.01
Blood Glucose (mmol/l)	14.5±1.20	5.6±0.58	<0.01
Glycosylated haemoglobin (%)	6.79±0.62	4.53±0.17	<0.01

DISCUSSION

The role of visfatin in development of type II Diabetes Mellitus is well established entity supported by many researches.[2–5] However, the concept of raised serum visfatin levels at early (4–12 weeks) of pregnancy in the women who subsequently develop gestational diabetes mellitus (GDM) is new.[7,9] Although the source of circulating visfatin in obesity and diabetes is visceral fat but some other studies support the fact that placenta may be implicated in raised serum concentration of visfatin in gestational diabetes.[8] During the course of normal pregnancy, the resistance to insulin increases physiologically and many studies suggest that visfatin possesses insulinomimetic properties.[10,11] which enables visfatin to bind to insulin receptors and increase intracellular uptake of glucose thus, leading to conclusion by Liang *et al,* that visfatin has an association with metabolic disorders of lipids, insulin and glucose in GDM.[12] This finding is consistent with our study finding that visfatin starts increasing in as early as first trimester of the pregnancy[7] and shows an increasing trend near term. However it has no association with parity or number of pregnancies whether primipara, multigravida, or grand multigravida.

Raised visfatin levels in GDM may be the reflection of impaired action of visfatin on receptors of target cells leading to dysregulation of glucose and lipid homeostasis leading to development of GDM.[13] Placental tissue could be a source of visfatin over secretion in GDM as one study shows the increased expression of visfatin receptors on placental tissue, mesenchymal cells, amniotic epithelium, parietal decidua and chorionic cytotrophoblastic cells.[14] We also found increased association of GDM and high serum visfatin levels in obese and overweight women with high BMI as compared to normal and underweight women as found by other researchers in recent past.[12]

There is some controversial role of visfatin and other adipocytokines in the development and progression of GDM as reported by Park *et al*, who studied 215 patients of GDM and 531 normal pregnant women and found reduced circulating visfatin and adiponectin level in GDM as compared to the normal pregnancy[15] while this finding was not showing consistency of results with our study where serum visfatin levels were significantly related to BMI and maternal obesity. We cannot draw a conclusion whether raised serum visfatin is a cause or consequence of gestational diabetes. This might be a limitation to the study where we can use visfatin as a biomarker for early detection of gestational diabetes. Study of Kiran *et al*, revealed that levels of visfatin in GDM women were elevated than women who showed normal glucose tolerance, a finding consistent with our study.[16] When the patients were further stratified trimester-wise we found high percentage of impaired glucose intolerance

in first trimester as compared to the second and third trimester GDM cases.

Recent studies have shown that visfatin increases weeks before the onset of gestational diabetes and can be of predictive value of the onset of disease not necessarily consistent with the maternal other characteristics. This is similar to a report which found increased visfatin levels weeks before clinical diagnosis of the disease.[1,7] Finding the difference of serum visfatin in GDM and Non GDM is a challenging finding in medicine and obstetrics, leading the researchers to find out an effective, simple, cost effective and less invasive techniques for diagnosis of GDM and many used saliva instead of serum and found a quite significant difference in both groups again showing a relationship between the two variables.[17] The focus of previous studies was primarily on the complex relationship between serum visfatin and Type 2 Diabetes Mellitus[18,19] which now shifts to the GDM in obese women, a finding consistent with our study and supported by international literature.[20]

CONCLUSION

Considering that visfatin participates indirectly in the development of GDM in obese women, visfatin might be a potential predictor for assessing GDM with obesity. Early screening for GDM is effective strategy for reducing the foetal and maternal comorbidities. The sample size limits the generalization of this study, so further well-designed epidemiological studies with larger sample size and strict stratification of other potential confounding factors should be done in order to fully understand the complex pathophysiology of visfatin in gestational diabetes prediction and therapeutics.

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ORIGINAL ARTICLE
CLINICAL SPECTRUM AND OUTCOME OF CHILDREN PRESENTING WITH POISONING TO TERTIARY CARE HOSPITAL

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Background: Accidental poisoning is one of the important emergencies in children. The objective of this study was to enlighten the clinical spectrum and outcome of poisoning in children presenting to a tertiary care hospital. **Methods:** This retrospective study was done in one of tertiary care hospitals, from Jan 2018 to Dec 2019. Retrieved from data, children of either sex aged from one month to 13 years admitted with diagnosis of accidental poisoning were included. Patients' age, sex, poisoning product, presenting symptoms to hospital and outcome from hospital as discharge, expired, transfer out, or left against medical advice were documented. Analysis of data was done using SPSS-20 and $p<0.05$ was taken as significant. **Results:** There were 51 patients, 33 (64.7%) males and 18 (35.3%) females. Patients' mean age was 4.24±3.6 years (Range: 1 month to 13 years). Children up to two years of age accounted for 45.1% of patients. The majority (41.2%) of poisoning was due to organophosphorus compounds. Opioids were major type of poisoning in younger children. The most common clinical presenting feature was vomiting and diarrhoea in 45.1% patients followed by the other presenting feature of respiratory difficulty which was present in 21.6% patients. Antidote was given in 68.6% patients. Out of 51 patients, 45 (88.2%) got discharged, 4 (7.8%) expired while 2 (3.9%) were transferred to other hospitals. **Conclusion:** Young male children are more at risk of poisoning. Organophosphorus compounds are leading cause of poisoning and the most common presentation is with vomiting and diarrhoea.
Keywords: Children, Poisoning, Organo-phosphorus Compounds, Kerosene oil

INTRODUCTION

Poisoning in children is one of the common emergencies.[1] Children can present with history of accidental ingestion of poisonous substances or inhalation of harmful substances.[2] It is one of the important preventable aetiology of morbidity and mortality in children as mortality due to acute poisoning is 3,000 per year in children younger than 14 years.[3] It is being reported that there in increase in incidence of poisoning in children due to lack of supervision and vigilance by elders, behavioural issues in children, easy accessibility to different poisonous substances, multiple health products and drugs, and increased media viewing.[4] Different studies have shown variable incidence of poisoning in children ranging between 0.3% to 7.6%.[5] Regardless of clinical spectrum of poisoning, it is always an emergency in paediatric patients. Children of age 1 to 5 year are more prone for poisoning due to more activity and curiosity. They tend to explore the environment around them due to less mobility and inexperience. With increase in age and cognitive development, the incidence of accidental poisoning decreases.[6]

Majority of children who present with history of poisoning, only require symptomatic treatment but a few patients may require immediate and specific treatment including antidotes to prevent the sequel of poisoning.[7] Management of poisoning in children include gastric lavage, decontamination, giving activated charcoal, specific antidotes and supportive treatment.[8]

It is important for emergency doctor working in paediatric emergency to have knowledge about the poisoning substances and their effects on body along with presenting clinical features whenever patient is being evaluated.[9] It not only saves life of patient but also leads to teaching and training of young doctors, nurses and paramedics.

Reasons of accidental poisoning in children are different in different countries and age groups. The knowledge of different poisoning substance and clinical spectrum in children can help in planning and taking care of paediatric patients. The objective of this study was to enlighten the clinical spectrum and outcome of poisoning in children presenting to tertiary care hospital.

METHODOLOGY

This study was performed in Paediatrics Department of one tertiary care hospital in Khyber Pakhtunkhwa. The data was retrieved from the records of patients admitted from January 2018 to December 2019 after approval from Institutional Review Board. The calculated sample size was 51 patients taking the incidence of poisoning in children as 3.40% and using Open-Epi sample size calculator.[5] Children of either sex from one month to 13

years age who got admitted with diagnosis of accidental poisoning (ingestion, inhalational, injection, contact) were included in the study. Children who got admission with intentional poisoning, poisoning due to foreign body ingestion, or aspiration or food poisoning were excluded. Patients with incomplete medical records were not included in the study. Patients' age, sex, poisoning product, container in which the poison was stored or kept, presenting symptoms to hospital, treatment given in emergency, antidote given if required, parents knowledge about the poisoning substance and outcome documented as discharge, expiry, transfer out, or left against medical advice were recorded. Patients were categorized into three groups according to age. In group 1 children age on month to 2 years were included. In group 2 children aged 2.1 years to 5.0 years were included. In age group 3 children aged above 5.1 years were included. Recorded data was analysed on SPSS-20 and $p \leq 0.05$ was considered statistically significant.

RESULTS

There were total 51 patients in this study. Out of 51 patients, 33 (64.7%) were male and 18 (35.3%) were female. Age of the patients ranged from 1 month to 13 years with mean age 4.24±3.6 years. The most affected age group was of children up to two years of age accounting for 45.1% of patients, followed by children age group 2–5 years, which had 25.5% patients. Children aged above 5 years accounted only for 29.4% patients. The most common poisonous substances taken were organo-phosphorus compounds including insecticides and rat killer poisons in 41.2% of patients. The other leading causes of poisoning were pharmaceuticals (antiepileptic drugs, benzodiazepines) and kerosene oil. Opioid poisoning was also an important cause but it was mostly in younger children in whom parents gave as remedy for treatment of acute respiratory infections (Table-1).

The most common container in which the poisonous substance was stored was either tablet pack or bottle as it was in cases who had used drugs. Cold drink bottles were the containers in case of kerosene oil poisoning. One patient presented with opioid poisoning with ingestion of cigarette containing cannabis from cigarette pack (Table-2).

The most common clinical presentation to hospital was vomiting and diarrhoea which was present in 45.1% patients followed by respiratory difficulty present in 21.6% patients. Respiratory difficulty was due to central respiratory depression and most of younger children were given opioids as cough remedy. Other features are shown in Table-3.

The majority of patients (51%) were given symptomatic treatment while gastric lavage was done in 31.4% patients. Gastric lavage was done in patients who

presented within two hours of ingestion of poisoning and it was not done in patients with kerosene oil or acid/alkaline poisoning. Activated charcoal was given in 5.9% patients and decontamination was done is 11.8% patients. Antidote was given in 68.6% patients while in 31.4% patients no antidote was required. Antidote included naloxone for opioids, atropine for organophosphorus, and oxygen for kerosene oil poisoning.

Out of 51 patients, 45 (88.2%) got discharged, 4 (7.8%) expired while 2 (3.9%) were transferred to other hospitals. All expiries were due to organo-phosphorus poisoning. Parents of only 27.5% patients had knowledge about the poisonous substance that how much it can be dangerous.

Table-1: Poison substances

Substances	Frequency	Percentage
Organo-phosphorus compounds/Insecticide	21	41.2
Plant/atropine	1	2.0
Opioid poisoning	9	17.6
Kerosene oil	9	17.6
Pharmaceutical drugs	11	21.6
Total	51	100.0

Table-2: Poisoning containers

Container	Percentage
Nil	39.2
Cold drink bottle	15.7
Glass	2.0
Tablet bottle/pack	29.4
Spray bottle	11.8
Cigarette packet	2.0
Total	100.0

Table-3: Clinical features at presentation

Features	Frequency	Percentage
Drowsiness	10	19.6
Vomiting diarrhoea	23	45.1
Breathing difficulty	11	21.6
Fever	1	2.0
Seizures	3	5.9
Vomiting, constipation	3	5.9
Total	51	100.0

DISCUSSION

As children grow, they have tendency to explore the surrounding environment, which at times can be hazardous. Though presentation with poisoning in children is not uncommon to paediatric emergency department, yet it is one of the important emergency visits. The paediatrician in emergency department must be familiar with common presentation of different poison substances and management.

Majority of poisoning is accidental in children and occurs at home; male children are more at risk for poisoning.[10] In this study children who presented with accidental poisoning were included. Majority of patients were male, which is comparable to the other studies. Studies have shown that children younger than 5 years of age are more at risk due to exploration

activity and curiosity for presentation with poisoning especially age group less than 2 years.[11] In our study 70.5% of children who got admitted with acute poisoning were up to 5 years of age and overall 45.1% children were up to 2 years of age. There were younger children less than 6 months with poisoning but parents gave them different plant derivative like opioid as remedy for treatment of acute respiratory infection. In one systematic review, Bhatta S et al[12] concluded that there is limited evidence that environmental change intervention reduces child injuries. Lee J et al[13] did a retrospective study in one of tertiary care hospital of Taiwan. In their study 52.3% children were male. The leading cause of poisoning was pharmaceutical drugs in 41.4% patients followed by pesticides in 9.5% patients. In our study the leading cause of poisoning was the organo-phosphorus compounds including insecticides, while second leading cause of poisoning was pharmaceutical drugs. The other two important causative agents of poisoning were kerosene oil and opioids. In Taiwan due to industrialization, more health products and drugs are available and parents kept at home, that's why Lee J, et al study the leading causes of poisoning are pharmaceutical products. Dayasiri MB, et al[3] did one study on plant poisoning in children in Sri Lanka. In their study 57% patients were male and 64% patients were less than 5 years of age. In their study 32% of parents did not know the severity of poisoning while in our study parents of 72.5% patients did know the nature of poisoning. Due to less education and lack of supervision by adults, majority of parents do not know that the poisoning in children can be hazardous. In Sri Lanka, the literacy rate is very high as compare to Pakistan that may be the reason parents are more aware of childhood poisoning hazardousness.

Khalid M, et al[14] in their study included 74 patients and males were 66%. In their study 54% of patients were between age of one and 5 years. In study 39% patients presented with ingestion of pesticides and 17.5% patients with kerosene oil poisoning. Where as in our study organo-phosphorus compounds including insecticides accounted for 41.2% cases and kerosene oil poisoning was present in 17.6% patients, which are almost equal to Khalid M, et al[14] study result as this study was done in Multan. Their study mortality rate was 16.2% while in our study morality was 7.8%. In our study, kerosene oil poisoning was one of leading cause of poisoning in children, as the poison container was the cold drink bottle. In our part of world cold drink are used frequently even by children especially during summer season. Kerosene oil is mostly used for cooking and also used in paints. So when parents keep it in cold drink bottles, children take it for cold drink and present with kerosene oil poisoning. In one of study by Hassan B, et al[15] in Egypt described poisoning due to petroleum products in 13% of patients. Ahmad I,

et al[16] in their study included 104 children, out of which 56% were male. The most common cause of poisoning was organ phosphorus compounds in 26% patients and kerosene oil poisoning in 21% patients, with overall morality of 4.8%. In one of study by Malla RR et al[17], 154 children were included. Out of 154 patients 57% were male and 43% were female. The most common poisoning was with Organophosphorus compounds (44.8%) while kerosene oil was in 13.63% and medicines were in 11.68% patients. Mortality was 1.29%. Omer HAM et al[18] studied the accidental poisoning in children in Yemen. In Omer HAM, et al study the most common poisoning was with kerosene oil which was present in 34.9% cases. One of study done by Obu DC et al[19] in Nigeria was regarding childhood poisoning. The study results showed male to female ratio of 2.3:1. In Obu DC et al the most common poisoning was with kerosene oil in 50% of patients and mortality was 5%.

Khan NU, et al[20] in their study checked for the trends of acute poisoning in children and adults. In their study 34.5% patients were children. The most common agents of poisoning in children were pesticides, hydrocarbons and pharmaceutical drugs. In our study also the common agents of poisoning in children were organo phosphorus compounds, pharmaceutical drugs and kerosene oil poisoning. Nisa B, et al[21] in their study included children with kerosene oil poisoning. In their study 75% of patients were male and in most of cases the kerosene oil container was plastic or cold drink bottles. Sanjeev RK et al[22] in their study checked for poisoning in children with carbamate which is one of organophosphate poison. It accounted for 21.88% poisoning cases. While in our study 41.2% patients were with organo-phosphorus poisoning. In study done by Abbas SK, et al[23], there were 46.5% less than 3 years of age while in our study 45.1% children were less than two years of age. The pharmaceutical drugs were the leading cause of poisoning followed by kerosene oil and organo-phosphorus compounds where as in our study organo-phosphorus compounds including insecticides were the leading cause of poisoning followed by pharmaceutical products and kerosene oil. In their study 7 patients left against medical advice while in our study none of patient left against medical advice. Memon Y, et al[24] in their study concluded that majority of children with poisoning were up to five years of age and kerosene oil poisoning was the most common form of poisoning. There was mortality of 3.22% in their study. In comparison in our study, majority of patients were up to five years of age but kerosene oil poisoning was third leading cause of poisoning. In our study the morality was 7.8%.

In another study done by Assar S, et al[25] in Iran described poising pattern in children as their study showed that majority of children were up to five years

of age. Opioids were the cause in 11.9% of cases as mostly in children less than 6 months of age. The common presenting features were vomiting in 50% of patients and decrease level of consciousness in 67% of patients. In our study opioids were one common cause in younger children as 17.6% of children presented with opioid poisoning. In our study the main resenting feature was vomiting and diarrhoea in 45.1% patients followed by breathing difficulty in 21.6% patients. Drowsiness as presenting feature was present in 19.6% patients. Poisoning is one of major cause of unintentional injury in young children with hydrocarbons, medicines and pesticides as common ingested agents.[26] Kumar et al[27] found 13.5% children with corrosive ingestion. In our study there was no patient with corrosive ingestion.

CONCLUSION

Poisoning in children is a common emergency in Pakistan. Male and young children are more at risk for poisoning. Organo-phosphorus compounds including insecticides along with pharmaceutical drugs and kerosene oil are leading poisoning materials in children.

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SSHS: Concept, design, data collection and writing
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ORIGINAL ARTICLE

CATHETER ASSOCIATED URINARY TRACT INFECTION DUE TO PROLONGED CATHETERIZATION AND ITS CAUSATIVE UROPATHOGENS

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Background: The presence of a urinary catheter is the most important risk factor for bacteriuria and Catheter-associated urinary tract infection (CA-UTI). The objective of this study was to determine the frequency of catheter associated urinary tract infections and most common causative uropathogens due to prolonged catheterization. **Methods:** This descriptive, cross-sectional study was carried out in the Department of Microbiology, Abbas Institute of Medical Sciences, Muzaffarabad from January to December 2019. Total 270 patients of critical patient care areas and wards with age range 18–70 years were selected. Patients suffering from UTI prior to catheterization, suffering from complicated UTI, and already catheterized at the time of admission were excluded. Urine samples were collected from the distal end of urinary catheters under strict aseptic techniques. Samples were cultured and growing microbes identified on the basis of gram stain, colony morphology, and biochemical reactions. **Results:** Catheter associated urinary tract infections due to prolonged catheterization of patients for more than 48 hours were found in 143 (52.96%) patients. The frequency of common causative uropathogens was: *E. coli* in 67 (47.18%), *Kleibsella* spp in 15 (10.56%), *Proteus* spp in 10 (7.04%), *Pseudomonas* spp in 8 (5.63%), *Staphylococci* in 14 (9.86%), *Enterococci* in 13 (9.15%) and other organisms in 15 (10.56%) patients. **Conclusion:** The frequency of catheter associated urinary tract infections with *E. coli* as the bacterial pathogen causing UTI due to prolonged catheterization is quite high.

Keywords: Catheter associated urinary tract infections, CA-UTI, *E. coli*, duration, catheterization

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INTRODUCTION

Urinary tract infections (UTI) are the most commonly acquired bacterial infections and they account for an estimated 25–40% of the nosocomial infections. The 70–80% of these infections are attributable to use of an indwelling urethral catheter.[1] As biofilm ultimately develops on indwelling catheters, the major determinant for development of bacteriuria is duration of catheterization.[2] The risk of urinary tract infection increases as the duration of catheterization increases. A patient with an indwelling urinary catheter has a 5% daily risk for development of urinary tract infection (UTI).[3] Catheter associated UTI (CA-UTI) occurs when urethral catheters inoculate organisms in the bladder and cause colonization due to providing a medium for bacterial adhesion and mucosal irritation. Urinary catheter is the most important risk factor for bateriuria.[4] Catheter acquired urinary infection is a source for about 20% of episodes of healthcare acquired bacteraemia in acute care facilities, and over 50% in long term care facilities.[2] Catheter associated bacteriuria is the most common health care-associated infection worldwide and accounts for up to 40% of hospital-acquired infections.[5,6] Most hospitalized patients are catheterized for only 2–4 days, but many are catheterized for longer durations.[7] About 5% to 10% of nursing home residents are managed with urethral catheterization, in some cases for years.[8] The bacteria may gain entry into the bladder during insertion of the catheter, during manipulation of the catheter or drainage system, around the catheter, and after removal.[9] The most frequently isolated uropathogen is *E coli* spp (31.7%).[10] Catheter associated urinary tract infections are associated with increased morbidity, mortality and adds 1–3 days of extra hospital stay.[11]

Implementation of an evidence-based 'UTI bundle' focused on the avoidance of catheter insertion, maintenance of sterility, product standardization, and early catheter removal can significantly decrease catheter-associated UTIs.[12] The rationale of this study was to determine the prevalence of catheter associate UTI in our population and emphasize the need to improve infection control practices for proper management of catheterized patients in hospitals.

METHODOLOGY

This descriptive, cross-sectional study was carried out in the Department of Microbiology, Abbas

Institute of Medical Sciences, Muzaffarabad from January to December 2019. Non-probability, consecutive sampling technique was used. Patients admitted in critical patient care areas and wards with age range 18–70 years were enrolled in the study after informed consent. Patients with underlying renal pathology or chronic renal disease, antimicrobial therapy and already catheterized at the time of hospital admission were excluded from the study. A total 270 patients of critical patient care areas and wards were included.

Two sets of urine samples were taken from every patient. First sample was taken to rule out any previous UTI on day zero, i.e., the day when catheter was inserted. Second sample was taken after 48 hrs from patients suspected of having CA-UTI with development of symptoms like fever and suprapubic tenderness. Urine samples were collected from the distal end of urinary catheters under strict aseptic techniques with sterile syringes, transferred to sterile urine containers, and sent to laboratory immediately.

Wet preparation of urine was examined microscopically for pyuria. Specimens were inoculated on Cystine Lactose Electrolyte Deficient (CLED) media (Oxoid CM0301) with filter paper strips that carry known amount of urine (0.2 uL). Culture plates were inoculated aerobically at 37 °C for 18–24 hours. Next day, plates were checked for growth of any uropathogen. In case of significant growth, i.e., colonies >15, the isolate was identified on basis of colony morphology, Gram staining, and biochemical reactions like catalase, coagulase, DNAse (in case of gram positive organisms) and oxidase test and Analytical profile index (API) 20E strips (bioMerieux.In) in case of gram negative organisms. Growth was observed and examined for 48 hrs. For the Quality Control, *E coli* ATCC 51153, *Staph aureus* ATCC 51153 and *Pseudomonas aeruginosa* ATCC 27858 bacterial strains were used. The Kirby-Bauer disc diffusion method was used to determine the antimicrobial susceptibility of isolates on Muller-Hinton agar using 0.5 McFarland standard, and disposable sterile swabs. Antimicrobial susceptibility and resistance was determined by isolate growth zone diameter according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Data was entered and analysed on SPSS-20. Mean±SD were calculated for quantitative variables (age and duration of catheterization). Frequency and percentages were calculated for qualitative variable like gender, CA-UTI and bacterial uropathogens. Effect modifiers like age, gender, duration of catheterization were controlled through stratification. Post stratification Chi-square test was applied and $p \leq 0.05$ was taken as significant.

RESULTS

In this study, a total of 270 patients were included. Age range in this study was from 18–70 years with mean age of 46.77±10.32 years. Out of these 270 patients, 179 (66.30%) were male and 91 (33.70%) were females with male to female ratio of 2:1. Mean duration of catheterization was 9.61±4.09 days Frequency of catheter associated urinary tract infections due to prolonged catheterization of patients for more than 48 hours was found in 143 (52.96%) patients. The frequency of the different causative uropathogens due to catheterization is shown in Table-1. Stratification of catheter associated urinary tract infections with respect to gender is shown in Table-2.

Table-1: Frequency of common causative uropathogens due to catheterization (n=142)

Causative uropathogens	Patients	Percentage
E. coli	67	47.18
Klebsiella spp	15	10.56
Proteus spp	10	7.04
Pseudomonas spp	8	5.63
Staphylococci	14	9.86
Enterococci spp	13	9.15
Others	15	10.56

Table-2: Gender-wise stratification of CA-UTI

Gender	Yes	No	*p*
Male	100 (55.87)	79 (44.13)	0.180
Female	43 (47.25)	48 (52.74)	

DISCUSSION

Catheter Associated UTI is defined as a symptomatic patient with a urinary catheter having one or more of the following symptoms or signs, with no other recognized infection: fever (temperature >38 °C), chills, catheter obstruction, abnormal urine colour or suprapubic tenderness, with positive urine culture with no more than two pathogens isolated.[13] Significant risk factors for CA-UTI include age, diabetes requiring insulin therapy, long hospitalization, and long duration of catheter insertion.[14] The impact of a UTI on the individual can vary greatly, depending on the age, comorbidities, and socioeconomic status. Moreover, it leads to unnecessary use of antibiotics and antimicrobial resistance and longer hospital stays.[15] CA-UTI is caused by instrumentation of the urinary tract and has been associated with increased morbidity, mortality, hospital cost, and length of stay.[16]

In this study, frequency of catheter associated urinary tract infections due to prolonged catheterization of patients for more than 48 hours was found in 143 (52.96%) patients. The most common causative uropathogens were Gram negative bacilli followed by gram-positive cocci. Our study was comparable with another study where Gram-negative

bacilli were the most common organisms (60%), followed by gram-positive cocci (36%) and then fungi (4%).[17] In another study from Turkey, biofilm producer microorganisms such as *E. coli, Psuedomonas aeruginosa, Klebsiellapneumonae, Proteus mirabilis* were significant cause of CA-UTI among catheterized patients.[18] The findings in our study were in concordance with other studies that also reported *E.coli* as the most common prevalent organism.[19,20] It is similar to Sayal *et al*[19] who reported that predominantly Gram negative isolates are seen in patients with prolonged catheterization.

It was found that patients catheterized for prolonged periods had significantly higher incidence of CA-UTI than those with shorter duration of catheterization. Higher prevalence of UTI associated with prolonged use of catheterization was similar to findings of Bello *et al*[21]. In a study of CA-UTI in nursing home residents, carried out by Brauer *et al*, it was found that *Proteus mirabilis*, *Enterococcus* spp, and *E. coli* were the three most common organisms causing CA-UTI.[22]

Another study showed CA-UTI in 68 out of 800 patients (8.5%) and the common organisms were: *Ecoli* (32.9%), *Pseudomonas* (15.1%), *Staph aureus* (12.3%), and *Candida albicans* (13.7%).[23] There may be many reasons for our rates to be on higher side, but the common reasons may be poor infection control practices and lack of policies for catheter insertion and maintenance. No strict adherence to bundle precautions to prevent UTI while insertion of urinary catheters was observed. Most of the staff is not trained for infection control practices. Moreover, there are no surveillance programs for CA-UTI and catheter use, and recommendations for quality indicators. Implementation of infection control practices, limiting placement and early removal of urinary catheters are powerful tools to improve rate of CA-UTI. Knowledge and attitude among nurses and doctors towards urinary catheterization and preventive measures related to catheter-associated urinary tract infection greatly affect the disease occurrence in patients.[24]

CONCLUSION

Longer duration of catheterization is significantly associated with higher prevalence of CA-UTI. *E. coli* is the most common bacterial pathogen causing UTI. CA-UTI prevention guidelines for reducing use and duration of catheterization and its proper management can help to overcome CA-UTI to a great extent.

RECOMMENDATIONS

Causative organism should be identified before starting any antimicrobial therapy in catheterized patients in order to decrease the resistance of uropathogens to antimicrobial agents.

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ORIGINAL ARTICLE

FREQUENCY OF ANTIMICROBIAL RESISTANT GENES IN *E. COLI* STRAINS PRESENT IN EFFLUENTS OF PHARMACEUTICAL INDUSTRIES IN PESHAWAR

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Background: The intense use of antimicrobial agents for the treatment of different infections resulted in bulk manufacturing of antimicrobial drugs by the pharmaceutical industries. The wastewater of these industries contains traces of raw form of antimicrobial agents which drains into sewerage system of the area, the exposure to which results in the development of resistant microbes. The goal of our study was to determine the frequency of antimicrobial-resistance genes (ARGs) in *E. coli* present in effluents of pharmaceutical industries in Hayatabad Industrial State, Peshawar. **Methods:** In this qualitative analysis 5 wastewater samples each were obtained from effluents of 5 different pharmaceutical industries situated at Hayatabad Industrial Estate, Peshawar. *E. coli* in these effluents was cultured and identified through biochemical tests and Gram staining. DNA was extracted and ARGs such as *sul1*, *dfrA1*, *tetA*, *tetB* and *ermB* were analyzed through Polymerase Chain Reaction (PCR). The results were tabulated in Microsoft Excel 2016. **Results:** *E. coli* were detected in the samples with citrate utilization and indole and triple sugar iron tests. The effluents contained resistant strains of *E. coli* which have developed ARGs against major antibacterials such as *sul1* for sulfonamides (84%), *dfrA1* for trimethoprim (80%), *tetA* and *tetB* for tetracyclines (80%) while *ermB* for erythromycin (72%). **Conclusion:** The wastewater effluents of pharmaceutical industries may be one of the major sources of development of ARGs in microbes.

Keywords: sul1, dfrA1, tetA, tetB, ermB, antimicrobial resistance

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INTRODUCTION

The word 'antibiotic' was introduced by Selman Waksman in 1941 who was an American scientist, meaning a molecule which is produced by a microbe against other microbes.[1] Since the discovery of first antimicrobial agent, their use for the treatment of infections is tremendously increased. Besides the beneficial effects, there are several concerns over the uncontrolled use of more effective antibiotics in our society. The major emerging concern is the emergence of resistance in suspected microbes against the most potent and efficacious antibiotics causing a major threat to public health and safety.[2] Antibiotic resistance is defined as 'the development of resistance in microbes against the action of antimicrobial agents'.[3] The main goal of antibiotic discovery previously was focused only against Gram-positive bacterial diseases, but now Gram-negative bacterial diseases are more concerning in research field for new antibiotics development. Antimicrobial resistance is developing rapidly in Gram-negative bacteria mainly due to presence of jumping genes on bacterial plasmid DNA.[4] Several microbes develop resistance against many chemotherapeutic agents, known as 'MDR' (Multidrug Resistant). Typical examples are *Mycobacterium Tuberculosis*[5], *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* and *Enterobacteriaceae* which are becoming serious health

problem now.[6] Antibiotic resistance develops mainly due to irrational prescribing, poor quality of drug formulation, water pollution and use of antibiotics in veterinary medicine and agriculture.[7] The bacteria acquire resistance against antibiotics through natural immunity, gene transfer mechanisms and plasmid-induced antimicrobial resistance.[8]

The presence of resistant bacteria in water ecosystems is an emerging problem worldwide. The studies performed on different water samples taken from different reservoirs like hospital wastewater, sewage-treatment plants, groundwater reservoirs and drinking water confirmed the presence of resistant species of *Enterococci*, *Enterobacteriaceae*, *Staphylococci* and other bacteria.[9] Even in the presence of water treatment plants, traces of antibiotics and resistant bacterial species could be very injurious to public health.[10] Patients treated with antibiotics excrete metabolites of these antibiotics in sewage water which enters water treatment plants and causes development of resistant strains.[11] As per study conducted in Nebraska State of America, anti-microbial resistant genes were found in streptococci and Gram-negative bacilli in surface water contaminated with human and animal faeces.[12] In Germany, Voigt *et al* confirmed the presence of MDR bacteria not only in sewage water but also in drinking water. In a recent study, waste-water treatment plants

and drinking water samples were investigated for presence of major Gram-positive and Gram-negative bacteria which may had acquired resistant genes through gene transferring mechanisms. The report revealed that these water sources are contaminated with resistant *Enterococci*, *Staphylococci*, *Enterobacteriaceae* etc. By using molecular biological tool like PCR, it was noted that these bacteria had acquired resistant genes against vancomycin, methicillin and other β-lactam antibiotics.[13]

Pharmaceutical industrial wastes containing antibiotics traces enter freshwater ecosystem from where water is used for community water supplies, putting the public at major health risk.[14] The aim of our study was to determine the frequency of antibiotic resistant genes in *E. coli,* i.e., *sul1*, *dfrA1*, *tetA*, *tetB* and *ermB* genes against major antibiotics groups including sulfonamides, trimethoprim, tetracyclines and erythromycin, in wastewater coming from Industrial Estate Hayatabad Peshawar.

MATERIAL AND METHODS

In this comparative study, water samples taken from industrial wastes were collected; treated water through Waste-Water Treatment Plants (WWTPs) was excluded from the study. A total of 25 random study samples were taken from 5 different industrial waste-water points at a depth of 0.5 m, and tested at Institute of Basic Medical Sciences, Khyber Medical University (IBMS-KMU) Peshawar. Presence of resistant *E. coli* in samples was confirmed by applying biochemical tests, i.e., citrate utilization test, indole test, and triple sugar iron (TSI) test. The *E. coli* was then cultured on MacConkey agar media and Gram staining was performed for identification of morphological features. *E. coli* colonies were recognized based on their morphological characteristics such as circular shape,

pink colour, raised, entire margin, and smooth and shiny texture. Glycerol stock solution was prepared for preservation of these bacterial colonies.

DNA from cultured bacterial samples was extracted by the 'Boiling lysis' method.[15] Specific primers[16] were prepared, and presence of antibiotic resistant genes (ARGs) was detected with PCR. The amplification products were analyzed by loading 10 µL of PCR product on 1.5% agarose gel in Bio-Rad PowerPac® electrophoresis system along with 1 µL of 6× loading dye, and 1000 bp DNA ladder was used for size discrimination. The results were then visualized under Accuris E3000™ UV trans-illuminator. The frequencies and percentages of ARGs present in resistant *E. coli* strains were tabulated and calculated on Microsoft Excel 2016.

RESULTS

The citrate utilization test was negative, i.e., the colour of the media remained green which showed presence of *E. coli* in the medium. A positive indole test was observed by finding red colour ring on the upper layer of media which indicated the presence of *E. coli*. The results of triple sugar iron test (TSI) also showed positive results, i.e., appearance of yellow slant in growth media. For presence of ARGs in isolated *E. coli* isolates, specific primers were designed for each type of resistant gene. There was a high mean percentage of *sul1* gene in *E. coli* strains (84%) in all wastewater samples obtained from effluents of selected pharmaceutical industries. Mean percentage of *dfrA1*, *tetA* and *tetB* resistant genes was found to be 80%, while mean percentage of *ermB* resistant genes was 72% in our study samples. The frequencies of different ARGS in our study samples are shown in Table-1.

The results were then visualized under ultraviolet (UV) trans-illuminator (Figure-1).

Table-1: Frequency of antibiotic-resistant genes in study samples

Sampling Site	*sul1*		*dfrA1*		*tetA*		*tetB*		*ermB*	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Pharmaceuticals A	4	80	5	100	4	80	4	80	5	100
Pharmaceuticals B	3	60	4	80	5	100	4	80	3	60
Pharmaceuticals C	5	100	5	100	4	80	4	80	3	60
Pharmaceuticals D	4	80	4	80	4	80	4	80	3	60
Pharmaceuticals E	5	100	2	40	3	60	4	80	4	80
Mean Percentage	84		80		80		80		72	
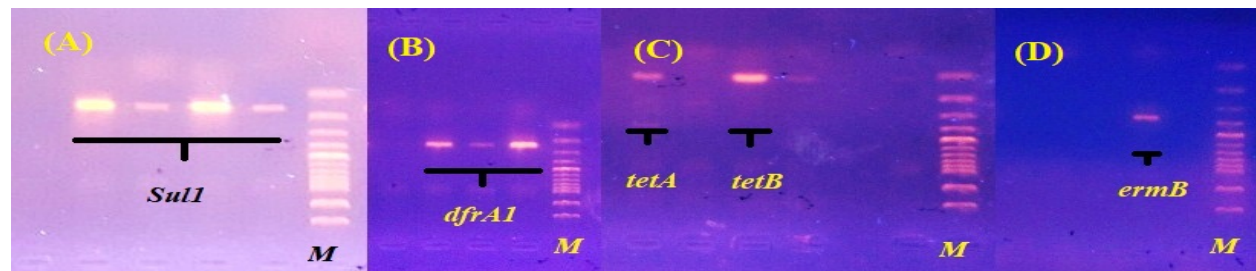
Figure-1: Antimicrobial Resistant Genes Amplification with 1000 bp DNA ladder
Left to Right: (A): *Sul1*, (B): *dfrA1*, (C): *tetA* & *tetB*, (D): *ermB*

DISCUSSION

Bacteria can acquire resistant genes sexually through the transfer of genetic material from one resistant bacterium to another non-resistant bacterium, i.e., conjugation, transduction and transformation mechanisms. This is known as 'horizontal evolution'.[17] Some bacteria transfer their genetically virulent genes to another species through bacteriophage viruses, which are responsible for horizontal gene transfer (HGT) from one bacterium to another.[18] Mobile genetic elements such as plasmids, transposons and gene cassettes, are also responsible for development of antibiotic resistance in bacteria.[19] Another mechanism by which bacteria can produce resistance against antibiotics is by the ways of efflux pumps, i.e., the pumping proteins that continuously kicks-out the antimicrobial agents out of the bacterial cell. Efflux pump is the major mechanism of antimicrobial resistance in *E. coli*, *Klebsiella pneumoniae*, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and other pathogenic bacterial species.[20]

Several classes of antibiotics are used for treatment of mild to severe infections such as penicillin, cephalosporins, macrolides, tetracyclines and aminoglycosides etc. Recently, synthetic antibiotics like carbapenems had become the drug of choice for the treatment of severe infections caused by *Enterobacteriaceae*.[21] Over the last 50 years, antibiotic prescription by healthcare professionals for treatment or prophylaxis against infections has increased.[22] Similarly, an increase in demand for animal protein in developing countries leads to the un-opposed use of antimicrobial agents in agriculture and fish farming business for better production. The antibiotic residues in these livestock products ultimately lead to antimicrobial resistance in bacteria.[23,24] To meet the demand, the production graph of pharmaceutical industries has also been raised. The industrial waste of such pharmaceuticals is mostly expelled through water in the drainage system.[25] Due to inefficient water treatment, the wastewater of these pharmaceutical plants is more likely to contaminate the freshwater reservoirs with antibiotics residues.[26] In developed countries, effective pharmaceutical wastewater treatment has reduced the risk of onset of antimicrobial resistance. However, the effective biological treatment systems themselves serve as an ideal place for growth of different microbes and even a low concentration of antibiotic residues may result in development of antimicrobial-resistant genes (ARGs) in bacteria on prolong exposure.[27] Guo *et al* found high frequency of ARGs in wastewater samples taken from different pharmaceutical wastewater treatment plants.[28]

Antibiotics resistance is now an emerging problem in Pakistan. Many studies performed at different areas of the country revealed resistance to antibiotics commonly prescribed for the treatment of infectious diseases. Self-medication and lack of knowledge about the use of antibiotics has lead to development of isolated resistant strains of *Streptococcus pneumoniae* against co-trimoxazole, amoxicillin and chloramphenicol in Pakistan.[29] The high frequency of antimicrobial-resistant genes in the microbiota of major water reservoirs of Pakistan like rivers, canal systems and also wastewater from pharmaceutical plants is a growing health concern. This includes ARGs against antibiotics like penicillins, tetracyclines, sulfonamides, macrolides, and fluoroquinolones.[30] The main reason for it is that the water treatment plants are not a priority of these industries. There are no regulations for levels of antimicrobials residues in wastewater effluents from pharmaceutical industries. This is because of a lack of data on minimum concentrations of antibiotics which may cause development of ARGs in microbes. Recently, some limits for antibiotic residues in pharmaceutical effluents has been proposed in Europe which requires effective implementation by drug regulatory authorities in developing countries.[31] A recent study conducted in Vietnam revealed that the pharmaceutical discharged water contains high concentrations of antibiotic traces including fluoroquinolones.[32] Antimicrobial resistance is a growing concern all around the world especially in developing countries due to lack of appropriate health control system. Sufficient measures are required to be implemented by the government for control of production and use of antibiotics in healthcare facilities.

In our study, a total of 25 water samples were taken from 5 pharmaceutical manufacturing industries for the presence of ARGs in *E. coli*. Our results showed that different samples of wastewater effluents of 5 pharmaceutical industries contain resistant strains of *E. coli* against antibacterials such as sulfonamides, trimethoprim, tetracyclines and macrolides.

CONCLUSION

The effluents of pharmaceutical industries situated in Peshawar are a source of producing resistant strains of *E. coli*. A high percentage of *sul1* resistant gene followed by *dfrA1*, *tetA* and *tetB* resistant genes, while a relatively low percentage of *ermB* resistant gene was found in their wastewater effluents.

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AM: Manuscript writing
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ORIGINAL ARTICLE
COMPARISON OF EFFECTS OF PROBIOTICS AND SITAGLIPTIN ON SERUM GLUCOSE IN DIABETIC RATS

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Background: Diabetes mellitus has become a major disease having catastrophic effects on health and economy globally. This study was conducted to determine the role of Probiotics in comparison to Sitagliptin in decreasing serum glucose levels in diabetic rats. **Methods:** Fifty male rats were divided into two groups: Normal control group-A (n=10) and Experimental group-B (n=40). Group-B was administered Streptozotocin to induce diabetes, which was confirmed after one week by measuring Fasting Blood Glucose (FBG) (>7 mmol/L were considered diabetic). Then group B was subdivided into BI (Diabetic Control), BII (Sitagliptin treated), BIII (Probiotics treated) and BIV (Sitagliptin plus Probiotics treated) with 10 rats each. Baseline serum glucose was measured at day zero. Next sampling was done on day 40, after administering Probiotics (250 mg/Kg) and Sitagliptin (10 mg/Kg). Terminal sampling was done on day 60. Statistical analysis was done on SPSS-21. Comparisons between the groups were analysed using one-way ANOVA (post-hoc Tuckey test), and $p<0.05$ was considered statistically significant. **Results:** Rats in Probiotic treated group-BIII had significant reduction in fasting blood glucose levels with efficacy comparable to Sitagliptin in group-BII ($p<0.05$). Synergistic effect of Sitagliptin plus Probiotics in group-BIV was greater ($p<0.05$) than their individual effects in groups-BII and BIII. **Conclusion:** Probiotics significantly decrease fasting blood glucose in diabetic rats with efficacy comparable to Sitagliptin. Synergistic effect of Sitagliptin plus Probiotics is greater than their individual effects.

Keywords: Fasting blood glucose, diabetes mellitus, Probiotics

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INTRODUCTION

Diabetes mellitus (DM) has become one of the major diseases in the world with its catastrophic effects on health and economy around the globe.[1,2] The burden of this disease has increased four times for the past three decades due to increase in obesity, sedentary lifestyle, consumption of high calorie food and ageing of population.[3] In the present era, there is rising trend of developing diabetes mellitus in childhood and adolescence.[4] Chronically disrupted metabolism in diabetic patients increases the risk for vascular complications and frequent hospitalizations.[3]

World health organization (WHO) reports around 171 million people globally are suffering from diabetes, with 82 million diabetic cases in the South East Asia.[5] In 2030, the diabetes prevalence will be 67%.[6] The Second National Diabetes Survey of Pakistan (2nd NDSP) 2016–17 reports, the prevalence of diabetes in Pakistan to be 26.3%, out of which 19.2% were old cases and 7.1% were newly diagnosed cases of diabetes. Diabetes prevalence in urban and rural areas has been reported as 28.3% and 25.3% respectively.[7]

Streptozotocin is used to induce diabetes in rat model, because it causes partial destruction of the beta cells. An inflammatory response is activated leading to auxiliary loss of beta cell activity and results in developing DM.[7] Oral dipeptidyl peptidase-IV (DPP-IV) inhibitors have emerged as newer hypoglycaemic agents which enhances the biological effects of incretin hormones by inhibiting their breakdown by dipeptidyl peptidase-IV enzyme.[8] Sitagliptin is the first oral DPP-IV inhibitor discovered recently.[9] Innumerable studies have established that Probiotics hold wonderful anti-diabetic activity and restore the action of pancreatic β-cells. Probiotics are safe, easily available, economical, eco-friendly, and provide a permanent cure of the disease.[10]

The treatment protocol of diabetes include both non-pharmacological (diet, exercise) and pharmacological measures (insulin and oral hypoglycaemic agents).[11] It is proposed that the modern approach to treatment of diabetes needs to be based upon prior identification of the cause and then treating the underlying biological abnormalities.[12] Therefore, the treatment approach towards diabetes should be to normalize or at least reduce the underlying physiological derangements in diabetes.

In a country like Pakistan, where a large population is living a life below the line of poverty, proposing expensive treatment strategies is not justified. Besides the economic constrains, the adverse effects of these medicines, prompt us to look for a safe alternative.[13] Use of Probiotics having good metabolic properties has the potential to be a better alternate

therapy for treating diabetes mellitus and its complications.[14] Limited data is available in Pakistan to highlight the uses of locally available commercial preparations of Probiotics. No study has been conducted so far for comparative analysis of Probiotics and Sitagliptin in Pakistan. This study will be a useful tool to bridge this gap in the field of diabetes management with commercial Probiotics preparations available for use by the society.

METHODOLOGY

This quasi experimental study was carried out at Pharmacology Laboratory, Multidisciplinary Research Laboratory, Islamic International Medical College, and National Institute of Health, Islamabad. Formal approval by the Ethics Review Committee of Islamic International Medical College, Riphah International University, was obtained for this work. The study was conducted from September 2020 to August 2021. A total of 50 male rats weighing 200–250 grams, without any physical abnormality and having normal baseline parameters were procured from NIH animal house.

All the rats were accommodated in standard cages at the Animal House of NIH, Islamabad. The rats had free access to tap water. Animal house atmosphere was maintained at 20 ± 2 °C with relative humidity of 50–70% and a light and dark cycle of 12 hours each. After acclimatization for 1 week, the rats were divided into two main groups; 10 rats were allocated to group A, and 10 rats each to group BI, BII, BIII and BIV. Group A was labelled as Normal Control whereas the group B (Experimental group) was administered single intra-peritoneal injection of streptozotocin dissolved in sodium citrate buffer at dose of 40 mg/Kg. Diabetes confirmation was done after one week in experimental group by measuring fasting blood glucose (FBG) and comparing it with Group A. Rats with fasting blood glucose >7 mmol/L were considered as diabetic.[1] The experimental group B was subdivided into four groups as BI, BII, BIII, and BIV.

Group A (n=10) had normal healthy rats with no intervention, having free access to food and water. Group B (n=10 in each group) had Streptozotocin induced diabetic rats, and were further subdivided into 4 groups. Group BI was diseased control group which did not receive any treatment and received normal saline with normal standard diet only. Group BII was diabetic rats which received Sitagliptin at the dose=10 mg/Kg/day.[15] Group BIII had diabetic rats receiving Probiotics at the dose=250 mg/rat/day[16] and Group BIV had Diabetic rats which received Sitagliptin (10 mg/Kg/day)[15] and Probiotics (250 mg/rat/day).[16]

A mid-cycle sampling was done after 40 days to see the progress of drugs on serum glucose levels. At day 60, final sampling of the experiment was done by cardiac puncture in all groups to see effect on serum glucose levels.[17]

Statistical analysis was done on SPSS-21. Results were documented as mean differences. Comparisons of quantitative parameters among the groups were analysed using one way ANOVA (post hoc Tuckey test), and $p<0.05$ was considered as significant.

RESULTS

Table-1 shows the comparison of Mean difference of all the groups. The results of group BII, BIII and BIV were compared to group BI, the diabetic control group. In the below mentioned table, the significant results are verified which are compared with the disease control group. In Probiotics plus Sitagliptin treated group BIV, there was a substantial drop in hyperglycaemia as compared to group BI, the diabetic control group. The results also imply that the synergistic effect of Sitagliptin plus Probiotics as a treatment tool for diabetes is greater than the effect of each drug individually in groups BII and BIII respectively.

Table-1: Comparison of mean difference of serum fasting blood glucose (mg/dl) in all groups on day 60

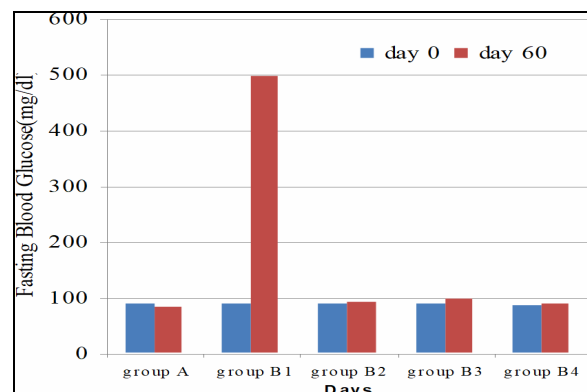| Groups	Mean difference	p
A *vs* B1	416.00	0.000*
A *vs* B2	10.10	0.04*
A *vs* B3	13.60	0.007*
A *vs* B4	6.00	0.21
B1 *vs* B2	405.90	0.000*
B1 *vs* B3	402.40	0.000*
B1 *vs* B4	410.00	0.000*
B2 *vs* B3	3.50	0.47
B2 *vs* B4	4.10	0.39
B3 *vs* B4	7.60	0.12

*Significant

Figure-1: Means of fasting blood glucose levels of all groups on Day 0 and Day 60 (n=50)

DISCUSSION

In present study, the anti-diabetic effect of Probiotics in comparison to sitagliptin is observed. Results of the present study confirm that hyperglycaemia induced by streptozotocin, is ameliorated by Probiotics with efficacy comparable to sitagliptin.

Various studies have reported that Probiotics have significant anti-diabetic effects.[18] Our study, revealed that the group treated with Probiotics had decreased FBG by reversing hyperglycaemia which is in agreement with Sohag MSU *et al*[19] who studied that administration of Probiotics decreased FBG in diabetic rats. Aggarwal J *et al*[20] studied the use of Probiotics and their anti-hyperlipidaemic action in streptozotocin-induced diabetic mice. A study by Yadav R *et al*[21] revealed that Probiotics supplementation improved metabolic profile in the diabetic subjects and caused reduction in their FBG, HbA1c and triglycerides.

No work has been done in Pakistan to compare the anti-diabetic effects of Probiotics with the anti-diabetic drug Sitagliptin. We chose Sitagliptin as it is a newer anti-diabetic drug with better qualities as compared to previous drugs.[22] Also the probiotic strain Lactobacillus has DPP-4 inhibitory activity like Sitagliptin, which was studied by Yan F *et al*[23]. This implies that their combined use will lead to synergistic effects in managing diabetes.

Most of the studies conducted for effects of Probiotics on diabetes were either on cultures of Probiotics[1] or Probiotics fermented products, e.g., probiotic fermented milk[24] or yogurt[25]. We used commercial preparation of Probiotic because of its easy availability. Such preparations are economical and for the sake of patient compliance they are easy to administer, i.e., via oral route. This was in accordance to a study conducted by Campos LF *et al*[16] who used commercial preparation of Probiotics with the name Protégé. The Protégé commercial probiotic preparation contained Lactobacillus and Bifidobacterium strains of Probiotics. Hiflora™, a commercial and locally available, probiotic preparation in Pakistan, that we used in our study also contained Lactobacillus and Bifidobacterium strains of Probiotics.

CONCLUSION

The synergistic effect of Sitagliptin plus Probiotics in lowering serum glucose in diabetic rats is greater than the effect of individual drugs. Probiotics significantly lower fasting blood glucose level in diabetic rats' model with efficacy comparable to Sitagliptin. Probiotics can be used as an adjunct in treatment for diabetes mellitus.

RECOMMENDATIONS

Comparative effects of different doses and roots of administration, besides other potential beneficial effects of Probiotics may be further investigated.

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SS: Design, methodology and review of content
RI: Revision of project and review of content
RM: Revision of project and review of content

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ORIGINAL ARTICLE
MICROBIOLOGICAL SPECTRUM OF UROPATHOGENS CAUSING URINARY TRACT INFECTIONS IN DIABETICS

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Background: Patients with diabetes mellitus (DM) are at increased risk of infections most commonly urinary tract infections. The objective of this study was to determine the spectrum of bacterial pathogens causing UTI in diabetic patients. **Methods:** A descriptive, cross-sectional study was carried out in the Department of Pathology, Abbas Institute of Medical Sciences, Muzaffarabad, from Jan to Dec 2019. A total of 292 patients with DM were enrolled in the study after informed consent regardless of the presence or absence of UTI symptoms. Patients with underlying renal pathology or chronic renal disease, pregnancy and antimicrobial therapy were excluded. Urine samples were taken and isolates were identified on the basis of colony morphology, gram staining, and biochemical reactions like catalase, coagulase, DNAse, oxidase test and Analytical Profile Index 20E strips (BioMerieux) as required. **Results:** A total of 292 patients were included. Mean age of the patients was 40.95±8.95 years. Out of these, 120 (58.90%) were male and 172 (41.10%) were females. The frequency of bacterial pathogens causing UTI was 37 (12.67%) for *E. coli*, 13 (4.45%) for *Klebsiella* spp, 5 (1.71%) for *Proteus* spp, 7 (2.40%) for *Pseudomonas* spp, 9 (3.08%) for *Staphylococcus aureus*, 7 (2.40%) for *Enterococci*, and in 214 (73.29%) patients there was no growth of any organism. **Conclusion:** *E. coli* is the most common bacterial pathogens causing UTI in diabetic patients.

Keywords: Diabetics, Urinary Tract Infections, UTI, Pathogens, Frequency

INTRODUCTION

Urinary tract infection (UTI) is common health problems in community as well as nosocomial setup and is usually caused by bacteria.[1] These infections range from asymptomatic bacteriuria (ASB) on one hand to acute pyelonephritis and gram-negative septicaemia on the other hand. Diabetes is one of the potential reasons of UTI[2], as sugar in the urine makes for a fertile breeding ground for bacteria and there is alteration in the immunity due to granulocyte dysfunction[3]. UTI is the most common infection among patience with DM and is responsible for considerable morbidity, particularly if it is untreated or unrecognized.[4] UTI in diabetic patients may lead to severe kidney damage and renal failure. Risk factors in patients are obesity, female gender, glycosuria, low immunity, and bladder dysfunction associated with DM.[5–7]

The spectrum of UTI in diabetics ranges from ASB to lower UTI (cystitis), pyelonephritis, and severe urosepsis. Mostly these patients are prone to resistant pathogens as the cause of their UTI, including extended-spectrum β-lactamase-positive Enterobacteriaceae[8], fluoroquinolone-resistant uropathogens[9], carbapenem-resistant Enterobacteriaceae, and vancomycin-resistant Enterococci.

Prevalence of UTI among diabetics is reported to be 25.3%.[10] The most frequently isolated uropathogens reported are *Escherichia coli, Klebsiella* spp, *Staph. aureus* and *Enterobacter.*[11]

There is no such data reported from northern areas of Azad Kashmir, especially for diabetics. The objective of this study was to evaluate microbiological spectrum of uropathogens causing urinary tract infections in diabetic patients of Muzaffarabad and surrounding areas.

METHODOLOGY

This descriptive, cross-sectional study was carried out in the Department of Pathology, Abbas Institute of Medical Sciences (AIMS), Muzaffarabad, from January to December 2019. A total of 292 adults (above 16 years) patients (both male and female) with DM who attend the outpatient and inpatient departments of AIMS were enrolled in the study after informed consent regardless of the presence or absence of UTI symptoms. Patients with underlying renal pathology or chronic renal disease, pregnancy, and antimicrobial therapy were excluded.

Patients were asked to provide a midstream urine sample according to clean-catch procedure. Sample was collected in sterile containers and processed within 1 hour of collection. Five ml of urine centrifuged at 3,000 rpm for 5 minutes was examined microscopically to detect WBCs, RBCs and bacteria. Urine analysis was done with dipstick test. Urine sample was inoculated on Cysteine lactose electrolyte deficient (CLED) agar with Bacteriuritest® strip (Mast Diagnostic) dipped in urine up to a defined mark (the strip picks 0.2 µL of urine). Plates were incubated for

18–24 hours at 37 °C under aerobic conditions and the outcome was judged as significant/non-significant growth or contaminated. Urine culture plates showing $>10^5$ colony-forming units (CFU)/ml of single bacterial species were considered as significant bacteriuria. Lower bacterial counts were considered insignificant and growth of more than two types of organisms was considered as contamination. MDR bacteria was defined as isolates resistant to >2 antimicrobial agents.

Isolates were identified on the basis of colony morphology gram staining and biochemical reactions like catalase, coagulase, DNAse (in case of gram-positive organism) and oxidase test and Analytical Profile Index (API) 20E strips (BioMerieux) in case of gram-negative rods. For the Quality Control, *E coli* ATCC 51153, *Staph aureus* ATCC 51153 and *Pseudomonas aeruginosa* ATCC 27858 bacterial strains were used. The Kirby-Bauer disc diffusion method was used to determine the antimicrobial susceptibility of isolates on Muller-Hinton agar using 0.5 McFarland standard, and disposable sterile swabs. Antimicrobial susceptibility and resistance was determined by isolate growth zone diameter according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Data was analysed using SPSS-16. Descriptive frequencies and percentages were computed for qualitative variables such as gender, marital status, level of education, type of DM, socioeconomic status, symptomatic and asymptomatic UTI, and bacterial pathogens. Mean and standard deviation were computed for qualitative variables. Stratification was done with regard for age, symptomatic and asymptomatic UTI, gender, type of DM and duration of diabetes mellitus to control effect modifiers. Post stratification Chi-square test was applied, and $p \leq 0.05$ was considered as statistically significant.

RESULTS

A total of 292 patients were included in this study. Mean age of the patients was 40.95±8.95 years. Majority of the patients (155, 53.08%) were >40 years of age (Table-1).

Out of 292 patients, 120 (58.90%) were male and 172 (41.10%) were females. The frequency of bacterial pathogens causing UTI was 37 (12.67%) for *E. coli*, 13 (4.45%) for *Klebsiella* spp, 5 (1.71%) for *Proteus* spp, 7 (2.40%) for *Pseudomonas* spp, 9 (3.08%) for *Staphylococcus aureus*, 7 (2.40%) for *Enterococci*, and in 214 (73.29%) patients there was no growth of any organism (Table-2).

Table-1: Age distribution of patients (n=292)

Age (Years)	No. of Patients	Percentage
16–40	137	46.92
>40	155	53.08
Total	292	100.0

Table-2: Frequency of uropathogens causing UTI in diabetic patients

Bacterial pathogens	No. of Patients	Percentage
E. coli	37	12.67
Kleibsella spp	13	4.45
Proteus spp	5	1.71
Pseudomonas spp	7	2.40
Staphylococci	9	3.08
Enterococci	7	2.40
No organism	214	73.29

DISCUSSION

Patients with diabetes are susceptible to infections (about four times more than non-diabetics)[12,13], which might be ascribed to their abnormalities in immune function.[14,15] Among the infections, urinary tract infections (UTIs) occur more frequently in diabetic patients[16,17] because of urine glucose excretion and chronic neurologic bladder dysfunction.[18] Furthermore, the prevalence of asymptomatic bacteriuria in diabetic patients is three times higher than in normal people; however, whether the symptomatic UTIs are preceded by ASB is unknown.[19,20]

UTIs may cause serious complications in diabetic patients, such as emphysematous cystitis, renal failure, bacteremia and papillary necrosis.[21,22] UTIs can also cause systemic inflammation and oxidative stress that elevate blood glucose and increase insulin resistance. Although the incidence of UTIs is higher and the severity of UTIs is more than anyone thought of previously, less than half of the UTI patients seek treatment in Asia.[23]

Escherichia coli is the frequent uropathogen in UTIs. However, the incidences of UTIs in different races and ethnicities are different. In previous studies, it was reported that the isolation of *E. coli* in European patients with UTIs was decreasing in the past 15 years.[24,25] The isolation rate of *E. coli* was 26% in Japanese patients with UTIs and 55.1% in Indian patients.[26,27]

Prevalence of UTI among diabetics is reported to be 25.3% in a recently published article.[10] Another study has revealed *Escherichia coli* in 13%, *Klebsiella* 13%, *Staph aureus* 9% and *Enterobacter* in 5%.[11] Fifty-seven percent diabetic patients yielded no growth.[11] Geerling has reported the members of the family *Enterobacteriaceae* (i.e., *Proteus, Klebsiella, Enterobacter,* and *Citrobacter* species), *Pseudomonas* species, *Enterococcus* species, *Streptococci, Staphylococci,* and *C. albicans*.[28] The emergences of resistant bacterial strains in hospitals pose a continued challenge to treat and control the spread of infections. Moreover, indiscriminate use of antibiotics often results in increased resistance of urine pathogens to most commonly used antimicrobial agents.[29]

Saber H, *et al*, in a study with a total of 288 diabetics (196 females and 92 males), and 63 non

diabetic patients (43 females and 20 males) with symptomatic UTI found that 43.8% diabetic patients and 42.9% non-diabetic patients had positive growth from urine. Same study shows rate of isolation of *Escherichia coli* in diabetics as 61.8% compared to non-diabetics (77.8%). Frequency of other organisms isolated in diabetic and non-diabetic patients in their study were respectively: *Klebsiella* spp 6.9% *vs* 3.7%, *Enterococcus* 12.2% *vs* 3.7%, *Pseudomonas* species 3.8% *vs* 0%, *Candida* species 4.6% *vs* 3.7%, *Staphylococcus aureus* 4.6% *vs* 7.4%.[30]

In our study, the organism associated with UTI was predominantly *E. coli*. The main reason for this is that the *E. coli* being the normal flora of gut gets easy access for UTI. These findings are similar to those observed by Boyko *et al*[31] on 218 diabetic postmenopausal women indicating that the prevalence of *E. coli* was 74.4% and that of *Klebsiella* spp. was 7%. Another case-control study, conducted in New Delhi, India, that evaluated the prevalence of UTI and renal scarring in 155 patients with diabetes, also found that *E. coli* was the most commonly involved organism (64.3%), followed by *Staphylococcus aureus* (21.4%) and *Klebsiella pneumoniae* (14.3%).[32]

Another study revealed that *E. coli* (49%) and *Enterococcus* species (35%) were the most prevalent pathogens followed by *Klebsiella pneumonia* (11%) and *Proteus mirabilis* (8%).[3] This finding is similar to other findings which indicate that gram negative bacterium, particularly *E. coli* remains the commonest pathogen isolated in patients with UTI.[33,34] In a study from Nepal, it was found that *Escherichia coli* was the most commonly grown organism (54.5%), followed by *Staphylococcus aureus* (17.3%), *Enterococcus* spp (9.4%) and *Klebsiella* spp (7.5%).[35]

In a study among 328 diabetic patients' urine samples, 34 (10.37%) showed culture positivity while out of same number of non-diabetic urine samples, 55 (16.77%) showed culture positivity. *E. coli* was found to be the most common isolated pathogen in diabetic and non- diabetic patients at 61.7% and 67.3% respectively. Other causative organisms of UTI in diabetic were *Klebsiella peumoniae* (14.70%), *Staph aureus* (11.77%), *Staph saprophyticus* (8.82%), *Pseudomonas aeruginosa* (2.94%), and in non-diabetic patients *Klebsiella pneumoniae* (5.45%), *Citrobacter freundii* (5.45%), *Klebsiella oxytoca* (3.63%), *Proteus mirabilis* (3.63%), *Providencia* spp. (3.63%), *Staph. aureus* (5.45%), *Staph saprophyticus* (1.82%), *Pseudomonas aeruginosa* (1.82%) and *Enterococcus faecalis* (1.82%).[36]

CONCLUSION

E. coli is the most common bacterial pathogen causing UTI in diabetic patients in diabetic patients of Muzaffarabad and surrounding areas.

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ORIGINAL ARTICLE

DIETARY PATTERNS AND RISK OF BREAST CANCER AMONG WOMEN: A CASE-CONTROL STUDY

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Background: Epidemiological studies have shown the robust link between breast cancer and dietary pattern. This study aims to examine the association of breast cancer with dietary patterns among Pakistani women. **Method:** This case-control study was carried out in multiple tertiary care facilities. Newly diagnosed primary breast cancer patients were recruited as cases (n=408); age matched controls (n=408) were randomly selected from the general population. Data on required parameters were systematically collected using subjective and objective tools. Factor and Principal Component Analysis (PCA) techniques were used to extract women's dietary patterns. **Results:** Four dietary patterns were identified based on eigenvalue >1; (i) veg-ovo-fish, (ii) meat-fat-sweet, (iii) mix (milk and its products, and gourds vegetables), and (iv) lentils-spices. Results of the multiple regressions were displayed as adjusted odds ratio (Adj. OR) and their respective confidence intervals (95% CI). After adjusted for potential confounders, veg-ovo-fish dietary pattern was found to be robustly associated with a lower risk of breast cancer among women (Adj. OR: 0.68, 95% CI: (0.46–0.99, $p<0.01$). **Conclusion:** Attachment to the diets majorly composed of fresh vegetables, and high quality protein sources may contribute in lowering the risk of breast cancer among women.
Keywords: Breast cancer, dietary pattern, women, principal component analysis

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INTRODUCTION

A tumour or lump in the breast resulting from abnormal cell division leads to cancer; its incidence has elevated over the last few decades.[1] A grave public health concern is posed by breast cancer (BC), which is the 2nd highest contributor to the cancer disease load around the world.[2] Globally, around 2 million women were the victim of BC in 2020, out of whom 0.7 million mortalities took place.[3] The rate of BC is expected to be increased worldwide by 46% up to 2040, and thus will be major cause for mortalities among women 2040.[4] Increasing trend in the BC has also been observed among all age women in Pakistan; every one in nine women falling into the disease at some point, have 2.5 times higher incidence than its neighbour and becoming Asia's country with the highest BC incidence.[5] Shaukat *et al*[6] reported that of all the cancers, 34.6% is contributed by BC. They suggested multiple attributable factors for the incidence of BC in different geographical settings.[6] Commonly reported factors include a broad list of socioeconomic and lifestyle related correlates of BC in different population and sites. In the recent past, behavioural modifications in dietary habits and practices have been observed in association with multiple non-infectious health disorders including BC. The most commonly reported diet related factors for BC incidence include straying away from traditional diets, intake of high animal-sourced foods, vegetable oils, refined sweeteners, and carbohydrates.[7]

Multiple observational studies on dietary characteristics and BC incidence among women have yielded inconsistent outcomes.[8] There has been negligible research in this area, specifically focused on dietary pattern among women with breast cancer, in the North-west region of Pakistan. This study aims to examine the association of BC with dietary pattern among Pakistani women to explore the women's attachment with different dietary patterns and the risk of BC in the North-west region of Pakistan.

MATERIAL AND METHODS

This case-control study was conducted at Out Patients Department (OPD) of Oncology Units after seeking ethical permission from the concerned bodies. Based on gender, oncologist-confirmed histology, and the presence of initial breast cancer, newly diagnosed (in the last one month) women were selected randomly. Same area residence, age-match (±2 years) were the prerequisites of the hospital and visitor-based controls. Both cases and controls were exposed to the same risk factors, and the controls were remarkably similar to cases in every aspect except for the presence of the disease. Samples from areas of diversified geography were selected with a sample size of 816 (408 each from cases and controls). Consent from the subjects was obtained. A structured questionnaire was developed on which interviews were conducted with the respondents, to collect data on multiple parameters and dietary characteristics. Women's anthropometric measurements including weight, height, waist and hip circumferences

were taken using standardized tools.[9] Body mass index (BMI) and waist to hip ratio were calculated.[10,11]

Data on usual dietary intake was collected using standardized food frequency questionnaire (FFQ). Dietary intake data was used to extract women's dietary patterns by Principal Component Analysis (PCA) and Factor Analysis (FA).

Data were entered into and analysed on SPSS-20. Data was checked for normality, and entry errors using descriptive statistics such as histogram, mean, frequency, mode, median etc. before analysis. Frequencies and percentages were calculated for categorical variables. Student's t-tests and Chi-square tests were used for the comparisons of means and percentages between the groups. Logistic regression models were used to identify dietary patterns in association with BC. Results of the regression models were expressed as odds ratio (OR) with 95% confidence intervals (CI) adjusted for potential confounders, and $p \leq 0.05$ was taken as statistically significant.

RESULT

Table-1 shows results on socio-demographic characteristics of the groups. Mean differences in age of cases and controls were non-significant. On an average, more cases compared to controls were formally illiterate (59% vs 41%, $p<0.001$). The occupational status indicates that 53% of BC patients were housewives and 33% were working women. Among healthy individuals, 47% were housewives, and 67% were working. There was a substantially significant ($p<0.05$) difference in women's position in occupations. Data regarding marital status showed non-significant differences which indicated that the incidence of breast cancer was also equally prevalent among single/unmarried and married women. Monthly income of the control group was marginally higher in comparison to cases ($p=0.06$). Results of the current anthropometric status of the groups show that BC patients had higher mean weight (Kg), BMI, waist circumference (WC), and waist-hip ratio (WHR) ($p<0.05$) as compared to healthy women.

FFQ data was used for identification of dietary patterns using PCA technique. Data suitability for the PCA (was confirmed by Kaiser-Meyer Olkin (KMO) and Bartlett's Test sampling adequacy measures. Based on a similar nutrient profile, the one hundred and forty-two FFQ food items were classified into 26 food classes. After running the PCA and FA, 4 dietary patterns were extracted based on eigenvalues >1. Factors were named according to the food items retained. Figure-1 shows the factor loadings of food items retained in each factors.

Associations of existing dietary patterns with the onset of BC were explored by running adjusted regression models (Table-2). Confounders included

women's BMI and WC. Women with high attachment (4th quartile) with the Veg-Ovo-Fish patterns were more protective for the onset of BC comparing to their counterparts. These findings remained same in both unadjusted and adjusted analysis (Adj. OR: 0.68, 95% CI: 0.46–0.99, $p<0.05$). No significant associations of other patterns with the BC were evident ($p>0.05$).

Table-1: Basic characteristics of the women by case/control status [n(%)]

Characteristics	Mean±SD/n(%)			
	Total	Cases	Controls	p
Age	816	45±6.3	45±2.7	>0.05
Education				
Illiterate	505	297(59)	208(41)	
<10 years	74	27(37)	47(63)	<0.001
10–12 years	141	51(36)	90(64)	
>12 years	96	33(34)	63(66)	
Occupational status				
Housewives	702	370(53)	332(47)	<0.001
Working women	114	38(33%)	76(67%)	
House hold Income (Rs ×1000)[a]	816	24±1.01	27±1.11	0.06
Marital status				
Single	86	38(44%)	48(56%)	0.15
Married	730	370(51%)	36(49%)	
Family size[b]	816	7.1±0.21	7.4±0.2	0.19
Anthropometric				
Weight (Kg)	816	64±13	62±12.4	<0.05
Body Mass Index (BMI)	816	24.4±5.0	23.7±4.1	<0.05
Waist Circumference (Cm)	816	82±7.7	80.8±7.7	<0.05
Waist to hip ratio (WHR)	816	0.80±0.0	0.79±0.0	<0.05

[a]Average income in KP (2010–11), i.e., Rs. 20,130, [b]Average family size in KP, i.e., 7
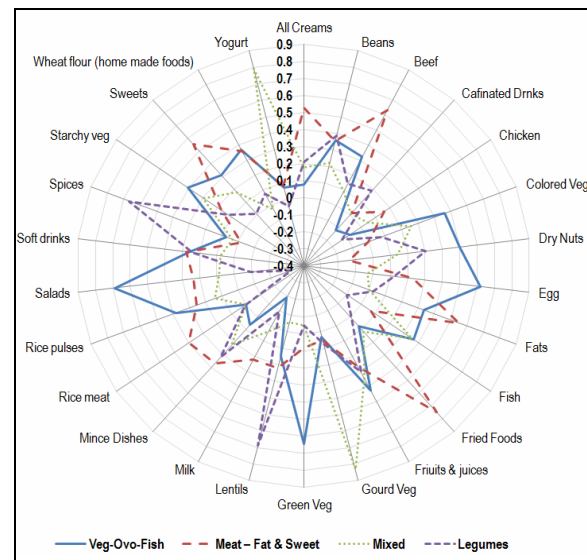
Figure-1: Rotated Factor Loadings of the extracted dietary patterns

a: For simplicity, only classes of foods or averages with absolute values greater than 0.2 were mentioned.

b: Factor scores are the same as a straight line between the food products and the factor. Higher scores mean that the food products have a greater proportion of variation in that factor. The orientation of each food item's relationship to the element is determined by the sign of the scores.

Table-2: Adjusted OR (95% CI) for breast cancer according to extracted dietary patterns

Dietary Pattern	Quartile	n (%)		OR (95% CI)	
		Cases	Control	Unadjusted	Adjusted*
Veg-Ovo-Fish	1st quartile	106 (26)	98 (24)	Reference	Reference
	2nd quartile	113 (28)	91 (22)	1.15 (0.78–1.69)	1.20 (0.81–1.78)
	3rd quartile	104 (26)	90 (24)	0.96 (0.65–1.42)	1.07 (0.68–1.49)
	4th quartile	85 (21)	119 (29)	0.66 (0.45–0.98)*	0.68 (0.46–0.99)*
Meat-Fat & Sweet	1st quartile	86 (21)	118 (29)	Reference	Reference
	2nd quartile	103 (25)	101 (25)	1.26 (0.51–1.12)	1.28 (0.86–1.89)
	3rd quartile	108 (27)	96 (23)	1.39 (0.94–2.06)	1.41 (0.95–2.10)
	4th quartile	111 (27)	93 (23)	1.34 (0.91–1.98)	1.34 (0.90–2.0)
Mixed Pattern	1st quartile	117 (29)	87 (21)	Reference	Reference
	2nd quartile	100 (25)	104 (25)	0.75 (0.51–1.12)	078 (0.53–1.16)
	3rd quartile	93 (23)	111 (27)	0.72 (0.47–1.03)	0.73 (0.49–1.08)
	4th quartile	98 (24)	106 (26)	0.73 (0.49–1.07)	073 (0.49–1.08)
Legumes-Spices	1st quartile	111 (27)	93 (23)	Reference	Reference
	2nd quartile	110 (27)	94 (23)	1.02 (0.69–1.50)	1.07 (0.72–1.60)
	3rd quartile	98 (24)	106 (26)	0.80 (0.54–1.18)	0.80 (0.55–1.23)
	4th quartile	89 (22)	115 (28)	0.70 (0.47–1.03)	0.70 (0.47–1.09)

*adjusted for body mass index, age, family size and total family income

DISCUSSION

Four dietary patterns, namely (i) Ovo-veg-fish, (ii) meat, fat, and sweets, (iii) mixed (gourd, vegetable, and dairy), and (iv) legume and spices, were identified in this study. Women's anthropometric measurements including BMI, age, family size and total household income were potential confounders for which adjustment were taken in the regression models. Attachment with the dietary pattern 'Veg-Ovo-Fish' was found a protective factor for BC in our study. A significant difference in percent women attached with this pattern was evident between the case-control groups. The food items in the current survey were chosen based on their availability and accessibility to the general population living in the study area. A diet constitutes balanced nutrients with diverse food groups such as whole grain (like rice and wheat flour), vegetables/fruits, meat, legumes, milk, and eggs to supply carbohydrates, proteins, fats, and other indispensable nutrients.

There is an association between eating vegetables and having a lower risk of breast cancer as they have anti-carcinogenic compounds like phytosterols, vitamins C and E, and beta-carotene providing protection by acting as antioxidants on oestrogen metabolism and reducing cell proliferation.[12,13] The results are statistically at par with a previous study which asserted that eating eggs raises free estradiol levels in the blood, resulting in greater breast cancer prevention.[14] The findings of one study that are similar to our study suggest that the long chain of omega-3 polyunsaturated fatty acids (PUFAs), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), inhibit proliferation by reducing epidermal growth factor receptor and human epidermal growth factor-2 signaling.[15] Dietary heme iron, lipids, and N-glycolylneuraminic acid which is found in red meat are thought to have the potential to boost tumour growth. Sugar has long been a staple of Pakistani cuisine. This is assumed to be linked to greater insulin sensitivity because of increased sugar consumption leading to higher risk of breast cancer.[16] According to a study, individuals who consume a lot of milk products are more likely to eat a lot of meat or other high-fat foods which can increase their breast cancer risk.[17]

Due to a population-based design, a relatively large sample size, together with other strict quality control measures (randomly matching cases and controls, regular evaluation on the quality of collected data, etc.), this study provides reliable evidence on the association of dietary patterns and breast cancer among Pakistani women. Nonetheless, we should keep in mind that the dietary data collected through face-to-face questionnaire interviews might not exactly reflect the real diet due to recall bias.[18] Even though all cases were newly diagnosed; it is possible that subjects will change their dietary habits after being diagnosed with breast cancer. However, women were asked for any modification in the frequency consumption of food items after being diagnosed. Available evidence on the possible mechanism of the observed associations of dietary patterns with breast cancer is still sparse and a potential protective effect of the traditional Pakistani pattern needs to be further studied.

CONCLUSION

Attachment to the diets majorly composed of fresh vegetables, and high quality protein sources may contribute in lowering the risk of breast cancer among women. The vegetable-ovo-fish dietary pattern may protect against breast cancer in women in Pakistan.

LIMITATIONS

The dietary questionnaire did not contain portion size, making it not possible to estimate nutrient consumption.

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ORIGINAL ARTICLE
FREQUENCY OF DENTAL ANXIETY AMONG CHILDREN AGED 5–12 YEARS VISITING A DENTAL TEACHING HOSPITALS IN KOHAT, PAKISTAN

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Background: Dental anxiety in children is recognized as a public health problem in many countries. Anxiety among dental patients directly affects their oral hygiene. The objective of this study was to evaluate the level of anxiety among children 5–12 years of age visiting dental hospital in Kohat city of Pakistan. **Methods:** This descriptive cross-sectional study was conducted on 400 children attending the dental teaching hospital in Kohat, Pakistan. 'Modified Child Dental Anxiety Scale' (MCDASf) was used to assess the level of anxiety in children. **Results:** Out of 400 participants, only 60 (15%) children were non-anxious, 119 (29.7%) were mildly anxious, 89 (22.2%) were moderately anxious while majority of the patients (132, 33%) were severely anxious. Statistically significant differences were observed between the level of anxiety and different age groups ($p<0.01$). As the age increased the mean dental anxiety score decreased from 20.70 in the age group 5–8 years to 16.35 in age group 9–12 years. **Conclusion:** Our study confirms age differences in dental anxiety and found to be lower in older age group. Strategies like recognizing the symptoms before starting any dental treatment and managing it with counselling and other therapies would have effect in reducing anxiety in younger age group.
Keywords: Dental anxiety, Dental fear, Dental treatment, Oral hygiene, MCDASf

INTRODUCTION

Dental anxiety is defined as 'An abnormal fear of visiting the dentist for preventive care or therapy and unwarranted anxiety over dental procedures'. Dental anxiety in children is accepted as a public health problem in several nations.[1] All these features affect a child's ability to deal with situation faced during the dental treatment.[2]

Anxiety from dental procedures is a common problem faced in dentistry that unfavourably affects the diagnosis as well as treatment.[3] Dental anxiety refers to a state of worry that something unfriendly is going to happen regarding the dental treatment and it is attached with a sense of losing control. This nervousness may be more distinct in relation to situations or objects clearly visible (e.g., hand piece, dental syringes).[4] Fear and anxiety associated with dental plan are one of the worries frequently faced by patients all over the world. Patients with dental anxiety usually have poor oral hygiene as they avoid their routine dental checkup.[5] Dental anxieties are ranked fourth among common fears and ninth among severe fears.[6] Studies have reported that poor oral hygiene and tooth loss are mutual in highly nervous patients compared to patients with low or no anxiety.[7] The frequency of dental anxiety in children in northern Europe is between 3 and 21 percent, and is more common among girls.[8]

There is inadequate material available on the occurrence of dental anxiety among children in Pakistan. A study was carried out in university students which show that around 23% of the adult population has high dental anxiety.[7] Another study carried out in Islamabad on similar age children where moderate and severe dental anxiety was seen in 38% cases.[9]

The purpose of this study was to evaluate the frequency of dental anxiety in children aged 5–12 years on visiting dental hospital in Kohat city, Pakistan.

MATERIAL AND METHODS

A total of 400 patients participated in our study. The sample size was calculated by using Epi-info sample size calculator with required 'Precision level' of 5%, 'Confidence level' of 95% and an estimated frequency of dental anxiety in children as 38%.

A questionnaire-based cross-sectional study was conducted in Khyber Medical University-Institute of Dental Science (KMU-IDS) from October 2020 to January 2021. Participants were selected by a non-probability consecutive sampling technique. The age of the participants in the study was between 5 and 12 years. They were accompanied by their parents/ guardians on visiting the hospital. Data was collected after informed consent from their parents and assent from the children. Children with known mental disorders and those who were not able to communicate were excluded from the study. The study population was divided into two groups based on age, i.e., 5–8 years and 8–12 years.

Ethical approval for the study was obtained from the Institutional Review Board (IRB), Khyber Medical University-Institute of Dental Science/Institute of Medical Science (Ref No. ERC/KIMS/2020/04). Written consent was obtained from all parents/guardian of the students who fulfilled the eligibility criteria.

The questionnaire used for the study was 'Modified Child Dental Anxiety Scale' (MCDASf).[10] It consisted of socio-demographic data with Corah's six items guide to measure the dental anxiety in children. Each item is five points Likert scale used to measure dental anxiety with score ranging from 'no problem' to 'very worried'. Total score on a scale ranged from 6 to 30. Dental anxiety was categorized on scores into 'No Anxiety' (6), 'Mild' (7–14), 'Moderate' (15–22) and 'Severe' (≥23).

Data was entered and analysed using SPSS-22. Descriptive statistics were run to calculate mean and standard deviation for age and dental anxiety score. Independent sample *t*-test was used to measure the association of dental anxiety in different gender and age groups.

RESULTS

Data from a total of 400 patients were collected in Dental Teaching Hospital in Kohat city. Among total, 217 (54.25%) patients were males and 183 (45.75%) were females. The mean age of the participants was recorded as 7.38±1.68 years. Majority (55%) of the children were in the age group 5–8 years compared to 8–12 years (45%).

Majority of the patients (36.9%) showed severe anxiety when asked 'How they would feel if their tooth had to be taken out', followed by 'Having a filling' (29.56%), and 'Having an injection in the gum' (28.6%).

Out of 400 patients, only 60 (15%) children were non-anxious, 119 (29.7%) were mildly anxious, 89 (22.2%) were moderately anxious, while majority of the patients (132, 33%) were severely anxious (Table-1).

The mean dental anxiety score was 18.65±6.61. The differences in anxiety level were not statistically significant between males and females (*p*>0.05). However, the differences were highly significant among age groups (*p*<0.01). As the age increased the mean dental anxiety score decreased from 20.70 in the age group 5–8 years to 16.35 in age group 9–12 years (Table-2).

Table-1: Level of severity of anxiety

Severity of Anxiety	Number	Percentage
No Anxiety	60	15.0
Mild Anxiety	119	29.7
Moderate Anxiety	89	22.2
Severe Anxiety	132	33.0

Table-2: Dental Anxiety Score by demographic characteristics (Mean±SD)

Characteristics	n	Dental Anxiety Score	p
Gender			
Male	217	18.40±6.87	>0.05
Female	183	18.90±6.35	
Age group			
5–8 years	220	20.70±5.88	<0.01*
8–12 years	180	16.35±6.25	
Total	400	18.65±6.61	

*Significant

DISCUSSION

Studies have reported that people having dental anxiety or fear dodge dental treatment and therefore live with oral health-related problems.[3] Dental anxiety remains an important issue for patients as well as dental clinicians despite modernization in pain management and dental techniques.[6] A recent study has associated dental anxiety with poor oral hygiene as well as poor oral health habits like unhealthy diet, less frequent tooth brushing and smoking which increase the need for involvements.[9]

One study from Islamabad[9] reported the prevalence of moderate and severe dental anxiety among children to be 38%. Another study from Peshawar[11] reported moderate and severe dental anxiety among children to be 68%. In our study 55.2% of the patients were moderately and severely anxious.

When compared with the other countries, the dental anxiety in children of Kohat was higher than those of Netherlands (6%)[10], Sweden (6.7%)[12] and Denish children (5.7%)[13]. Studies have suggested that there is a counter relationship between levels of dental anxiety and age.[14,15] In the current study dental anxiety was higher in the younger age groups. Older age groups reported lower mean MDAS score steady with previous work[10,11] which has reported an increase in anxiety score in the younger age group. This may be due to patience developed eventually by increased contacts and thus have less anxiety as they grow up.[16] In our study MDAS was not statistically significant with gender, which is not in accordance with other studies showing females had a higher mean MDAS score compared to male children.[17] It may be due to the culture of telling our young boys not to be afraid or cry like girls, and resultantly they hide their fear and anxiety.

CONCLUSION

Our study confirms age differences in dental anxiety and found to be lower in older age group. Strategies like recognizing the symptoms before starting any dental treatment and managing it with counselling and other therapies would have effect in reducing anxiety in younger age group. Social awareness programs related to oral health may be valuable in dropping dental anxiety.

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ORIGINAL ARTICLE
IMPACT OF PRIMING WITH THE HELP OF VIDEOS ON THE STUDENTS' LEARNING EXPERIENCES IN UNDERGRADUATE MEDICAL EDUCATION

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Background: Priming is an active learning approach which helps prepare a learner for an educational task. This study aims to introduce priming with the help of videos in undergraduate medical curriculum and to assess the perceptions of students regarding the impact of priming on their learning experiences. **Methods**: It was a questionnaire based cross-sectional study conducted for 3 months in 2020. Videos were introduced to 2nd year medical students in the Special Senses Module conducted online. Videos retrieved from authentic websites were posted, with due permission, and shared before the didactic session on a particular topic. At the end of module, perceptions of students were gathered via an online questionnaire, after consent. **Results:** Majority of students 'agreed' or 'strongly agreed' that priming is an effective way of learning (86%) and they would like to be provided with resources for priming in the future (90.7%). Sum 89.2% of the participants 'agreed' or 'strongly agreed' that they prefer priming with in class discussion over traditional teaching. Majority of the students 'agreed' or 'strongly agreed' that the video resources used for priming were conducive to their learning (92.2%), helped in better comprehension of the respective topics (93.8%), and would make it easier for them to revise for assessments (67.2%). **Conclusion:** This research supports the benefits of priming with the help of videos in undergraduate medical education. Using videos as a tool for priming helps in better comprehension of the topic and makes it easier for the students to revise for assessment.
Key words: Medical education, priming, videos.

INTRODUCTION

Priming means preparing or readying. In literature pertinent to education, priming refers to any intervention adopted to prepare a learner for an educational experience or task.[1] Priming can be used as an active learning strategy. Active learning is a method of enhancing student learning by involving the student directly in the learning process. Active learning is supposed to stimulate higher order cognitive functions of the students and motivates them to become self-regulated, independent learners.[2]

One of the priming techniques which can be used is by providing students with informational videos and making them view those videos prior to in-class didactic lecture and/ or small group discussion.[3] The use of videos in higher education is fruitful because of the ability to self-pace, engage with content through calculation, select tasks, and reflect and respond to questions.[4] Videos can have a significant effect on orienting learners to a new subject. Studies have shown that videos were considered as an easier media to learn from compared to primarily verbal content.[5,6]

Videos, as a form of e-learning, have been shown to effectively involve students in learning outside the traditional confines of the classroom.[7-9] Videos can be used to encourage active learning and allow reflection on student knowledge and understanding.[10,11] Kelly *et al* reported that the videos were positively received by students, however these videos did not

impact overall students' learning outcomes, concluding that they were a valuable adjunct to face to face sessions.[11] Other studies reported that videos have not only been positively received, but positively affect performance.[12,13]

This study was designed to further explore the impact of using video exemplars in an undergraduate medical curriculum. The objective of this study was to introduce priming with the help of videos to second year undergraduate medical students and to assess their perceptions regarding the impact of priming on learning experiences.

METHODOLOGY

This study was conducted at Shifa College of Medicine. Videos were introduced to the students of 2nd year MBBS in the module of Special Senses. It was a 3 week long module conducted in a hybrid manner (a combination of online and on campus activities) in July 2020 due to COVID 19. The Videos were retrieved from some of the authentic websites and were posted with due permission of the author. The videos were uploaded on the Google classroom before the didactic lecture, small group discussion and/ or practical session on a particular topic. The videos shared before a lecture or a small group discussion comprised of short animated lecture not exceeding 10 minutes and the ones shared before the practical sessions comprised of prerecorded demonstrations retrieved from the internet. At the end of

module, perceptions of the students were gathered via an online questionnaire, after taking consent. Likert scale from 0–4 was used for scoring with 0=Strongly disagree, 1=Disagree, 2=Uncertain, 3=Agree, and 4=Strongly agree. Data was analyzed on SPSS-21 and $p<0.05$ was considered significant.

RESULTS

Table-1 shows the results of survey questions which were meant to evaluate the acceptance of priming as a learning tool. 86% of the students agreed or strongly agreed that priming is an effective way of learning. 89.2% of the participants agreed or strongly agreed that they prefer priming with in class discussion over traditional teaching. 90.7% of the students agreed or

strongly agreed that they would like to be provided with resources for priming in the future.

Table-2 shows the results of the survey questions that were meant to assess the effectiveness of videos as a priming tool. 92.2% of the students agreed or strongly agreed that the video resources used for priming were conducive to their learning. 93.8% of the participants agreed or strongly agreed that the videos helped in better comprehension of the respective topics. As far as the impact on preparation for examination is concerned 67.2% of the students agreed or strongly agreed that provided videos would make it easier for them to revise for assessments / exams and 40.6% were neutral about it.

Table-1: Results of students' survey questions to evaluate the acceptance of priming as a learning tool

Questions	Strongly disagree N (%)	Disagree N (%)	Neutral N (%)	Agree N (%)	Strongly agree N (%)	Mean±SD
I made sure to watch all the videos provided for priming	1(1.6)	8(12.5)	16(25)	21(32.8)	16(25)	3.69±1.049
I made sure to watch the videos 'before' sessions	1(1.6)	10(15.6)	23(35.9)	21(32.8)	9(14.1)	3.42±0.973
Priming should be implemented for other modules	2(3.1)	0(0)	4(6.3)	25(39.1)	32(50)	4.35±0.864
Priming is an effective way of learning	0(0)	0(0)	7(10.9)	30(46.9)	25(39.1)	4.24±0.777
I would like to be provided with resources for priming in the future	1(1.6)	1(1.6)	4(6.3)	28(43.8)	30(46.9)	4.33±0.798
I prefer priming with in class discussion over traditional teaching	2(3.1)	0(0)	4(6.2)	27(41.5)	31(47.7)	4.33±0.858

Table-2: Results of students' survey questions to assess the effectiveness of videos as a priming tool

Questions	Strongly disagree N (%)	Disagree N (%)	Neutral N (%)	Agree N (%)	Strongly agree N (%)	Mean±SD
The video resources used for priming were conducive to my learning	0 (0)	1 (1.6)	4 (6.3)	30 (46.9)	29 (45.3)	4.36±0.675
The videos gave a broad overview of the topics	0 (0)	0 0)	4 (6.3)	40 (62.5)	19(29.7)	4.24±0.560
The videos promoted my desire to learn	1 (1.60)	1 (1.6)	18 (28.1)	28 (43.8)	16 (25)	3.89±0.857
The videos were relevant to the topics that they were provided for	0 (0)	0 (0)	1 (1.6)	33 (51.6)	30 (46.9)	4.45±0.532
The videos used for priming piqued my interest in topic	1 (1.6)	0 (0)	12 (18.8)	35 (54.7)	1 5(23.4)	4±0.762
The videos were fun / interesting to watch	0 (0)	2 (3.1)	10 (15.6)	29 (45.3)	23 (35.9)	4.14±0.794
The videos helped in better comprehension of the respective topics	0 (0)	1 (1.6)	3 (4.7)	35 (54.7)	25 (39.1)	4.31±0.639
The provided videos will make it easier for me to revise for assessments / exams	2 (3.1)	2 (3.1)	17 (26.6)	26 (40.6)	17 (26.6)	3.84±0.963
I felt the videos wasted my time which i could have spent reading the textbooks	12 (18.8)	39 (60.9)	6 (9.4)	3 (4.7)	2 (3.1)	2.10±0.882
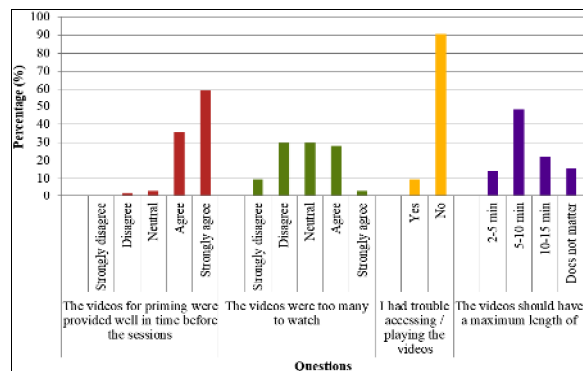
Figure-1: Results of students' survey questions to assess timing and accessibility of the provided videos

Figure-1 shows the results of students' survey questions to assess the timing and accessibility of the provided videos. 90.6% of the participants were of the view that they did not face any trouble playing the videos. 95.3%

of the students agreed or strongly agreed that the videos for priming were provided well in time before sessions.

DISCUSSION

The main goal of health professions education has gradually shifted over the years to attaining competencies by the students through self-directed learning and this is encouraged by the active learning strategy. 'Priming' of the students is one such active learning approach.[2] Priming is a component of the flipped classroom which is a novel educational approach. In this teaching model, students have to do 'homework' before the class in order to utilize the class time for a more interactive and engaging session.[14] 'Priming' means prior exposure to a topic for better understanding and learning. In this study, we primed the students through videos on a particular topic on which the didactic lecture was not yet conducted.[2]

In our study majority of the students agreed or strongly agreed that they found priming to be an effective way of learning and they would like to be provided with resources for priming in the future. This is in concordance with a study conducted by Bhandari *et al*, where the students' evaluated the 'self-priming 'process as an effective way of learning, which helped in better orientation and better comprehension during didactic class-room lecture on the topic.[2] Similarly, in another study by Rose *et al*, sixty-two percent of students surveyed preferred the priming with in-class discussion model to a traditional lecture format.[14]

Priming can be done in a number of ways. The priming model which we introduced in our study was with the help of online videos which were provided before the didactic lecture on a particular topic so as to utilize the class time for discussion. In our study majority of the students agreed or strongly agreed that the video resources used were conducive to their learning and piqued their interest in the particular topic. A study conducted by Botelho *et al* revealed similar findings where students perceived videos to be an important learning tool and most of the students were of the opinion that video learning materials allowed students to clarify concepts and enhance cognitive thinking.[15]

In our study 89.2% agreed or strongly agreed that they prefer the teaching format with priming before the class and utilization of the class time for active discussion over the traditional teaching format. This finding is similar to the findings of a meta-analysis conducted by Hew KF in 2018, where 70% of the total respondents reported that they preferred flipped classroom over traditional classroom. The studies included in the meta-analysis used pre-class flipped classroom activities including at least the use of instructor-recorded classroom lectures, Power Points with instructor talking head, Power Points with instructor's voice over, YouTube videos, Khan Academy videos, TED (technology, entertainment, design) video talks or screencast.[17] In another study conducted by Kugler AJ *et al* in 2019, most of the students indicated that their overall experience with the flipped classroom format using pre-recorded videos was either positive or neutral, and a lower percentage of students considered the experience to be negative. However, when asked about whether the flipped classroom technique was more beneficial than the traditional teaching methodology, survey respondents were split almost evenly (agree or strongly agree=48.9%, disagree or strongly disagree= 51.1%).[16]

In our study majority of the students agreed or strongly agreed that the provided videos helped in better comprehension of the respective topics and would make it easier for them to revise for assessments / examinations. This was in accordance with another study carried out by Fong KK *et al* in 2020, which revealed that overwhelming majority (92.1%) reported that the videos increased their sense of preparedness for the examination.[18] We suggest that priming should be implemented in undergraduate medical education to encourage active learning among students.

CONCLUSION

This research supports the benefits of priming with the help of videos in undergraduate medical education. Using videos as a tool for priming helps in better comprehension of the topic and makes it easier for the students to revise for assessment.

LIMITATIONS

This qualitative study was carried out in a single institute; therefore, the results cannot be extended to other populations.

FUTURE SUGGESTIONS

Further studies are needed to determine the effects of priming with the help of videos on academic performance of the students.

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ORIGINAL ARTICLE
ROLE-PLAY: A SIMULATED TEACHING TECHNIQUE IN PHYSIOLOGY

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Background: Simulation is an artificial representation of a situation to facilitate learning without the risks inherent in a similar real-life experience. Role-play is one type of simulation that focuses attention on the interaction of students in scripted scenarios. In the process, students learn about that patient or given situation. This study was conducted with an aim to record the response of undergraduates to role-play of clinical scenarios and to have their feedback. **Methods:** Two clinical topics were selected from second-year MBBS Physiology syllabus and assigned to two groups of students, having 7 students each. Case scenarios were formulated; scripted and roles were divided among students. Role-play of each scenario was followed by a presentation on the pathophysiology. Student feedback was recorded and analysed. **Results:** Out of the 137, 56 (40.88%) were male and 81 (59.12%) were female students who participated in the study, 50.4% considered role-play alone as a useful learning tool whereas 94.9% agreed that if role-play is combined with a multimedia tool then it is useful for learning (χ^2=110.43, $p<0.001$). 95.9% said that role-play is enjoyable (χ^2= 114.07, $p<0.001$) and 97.1% said that it is a good technique to improve communication skills (χ^2= 121.46, $p<0.001$). Regarding future interest in more role-play scenarios, 56.9% of the study participants said they will be very interested. **Conclusion:** Hence, concluded that with careful planning and utilization of resources, role-play has the potential to be incorporated in the teaching of clinical scenarios to undergraduates to promote learning.
Keywords: Role play, simulation, medical education, undergraduate physiology teaching

INTRODUCTION

Simulation is a rapidly evolving and promising pedagogical tool used to impart knowledge to students. It is the art of achieving goals and learning objectives[1] through artificially replicating sufficient components of a real-world situation[2] without associated risks and harms[3]. It aims to further the learning of skills or knowledge by enabling immersion of the learner, making them self-reflect[4] through facilitating the process of feedback, and by putting the acquired skills or knowledge into practice[5]. Historically speaking the first use of simulation in healthcare was in nursing education employing Mrs. Chase, a full-sized doll in 1911 while use in aviation and military came into play in the form of early flight simulators being built in 1927.[6] Simulation transcends from the undergraduate to graduate level, pre-clinical to the clinical setting, and beyond. It is a teaching strategy that is evidence-based contextual learning that promotes and facilitates experiential learning and helps the student to foster clinical reasoning and analytical thinking. Simulation can be used to help bridge the gap between theoretical knowledge and practice which could have been hindered previously due to safety concerns that are normally present in a real-life situation.[7]

The degree of realism and technical complexity offered by a particular simulation is termed as its fidelity.[8] On the fidelity continuum, a question stem describing the patient's signs and symptoms or a clinical scenario that expects from the examinee to reach a relevant clinical decision is a type of simulation which is at the lower end. Assessments that employ standardized patients are however at the opposite end of the fidelity spectrum, providing a more tangible method for quantifying the clinical competency and skills of the student in question.[9] Simulations, be it low fidelity or high fidelity allow for the user to develop clinical skills safely in a healthcare setting. When used by undergraduate medical students during the degree duration, they are able to acquire clinical skills by practicing on the different modalities, which they would otherwise gain in medical practice at the risk of causing medical error-related deaths.[10] Deaths caused due to medical negligence are the third leading cause of death in the US, amounting to almost 400,000 per annum.[11] High-risk clinical situations when learned and practiced through simulation can significantly enhance patient management and outcomes for the better in real-life situations, for instance, a study that explored the septic shock resuscitation knowledge and confidence of students concluded that the simulation improved both aspects for learners and equipped them better for real-life scenarios.[12]

Simulations could be compiler-driven mimicking a part of the physiology or anatomy such as intravenous-insertion arms or urinary catheter trainers. Or simulations could be event-driven standardized patients; these are professionals who have been trained

to play out the roles of patients who provide history and undergo physical examinations during a clinical case role-play.[5] Historically role-play emerged from psychodrama. It calls upon participants to play the scenario. It is a type of experiential learning in which participants take on different personas and navigate through a scenario that is set to mimic the real situation, doing this all the while in their assumed roles. To simply put, role-play is a form of art in which you ask of someone to imagine that they themselves or someone else is in a particular situation. The imaginer is then called on to behave exactly as they feel that the said person would in the supposed scenario. Consequently, this would translate into them or the rest of the class, or both[13], learning something about the person and/or the situation.

Role-play helps the students to develop certain soft skills such as understanding, better communication skills[14], empathy[15] and to pick up on verbal and non-verbal cues which are not stated overtly in an actual clinical setting[16]. Role-play enables students to become more mindful and has been proved to increase activity pertaining to elicitation, externalisation, and consensus-building.[17] Through simulation-based learning such as role-play, team reflexivity could be increased leading to increased collective competence of healthcare teams.[18] When compared to other simulation-based teaching methods, role-play turned out to be an economical and cost-effective method to engage students in active learning.[19] Role-play was also reported by students as an effective method to teach them on how to manage workplace conflict.[20]

In the light of the potential benefits of role-play, as a teaching method, such as sharpening the skills of expression, becoming observant, pragmatic, and analytical, providing exposure to the complicated and complex nature of real-life problems, and increasing empathy for individuals who undergo these circumstances in real-life, the study was conducted with an aim to record and assess the response of MBBS undergraduate students to role-play of clinical scenarios during the teaching of Physiology at CMH Lahore Medical College and Institute of Dentistry.

METHODOLOGY

This descriptive cross-sectional study was conducted in the Department of Physiology, CMH Lahore Medical College during an ongoing academic session of 2nd Year MBBS after seeking approval from the institutional Ethical Review Board. Two clinical topics were selected from Endocrinology and Renal Physiology and two groups of students were allocated these topics purely on a voluntary basis. Case scenarios were formulated, scripted, and specific roles were divided.

Role-play on acute renal failure was based on a scenario in which a young boy ate mushrooms on a hiking trip, developed lethargy, confusion, rashes, and pain. The boy was brought to the doctor for an examination and the doctor explored the possible diagnosis through history taking and physical examination. While the actors played out their roles, the rest of the class watched how the scenario unfolded. The role-play scenario on hyperthyroidism was presented to the whole class in a similar way along with an oral presentation of the pathophysiology of the disease on PowerPoint and Prezi. Factors that make a session interesting were incorporated into the scenarios. The actors used a variety of expressions using verbal and paraverbal communication. The conversation was kept interesting and the performance of clinical methods was incorporated to break the monotony. There was a reinforcement of concepts in the script and in the presentation that followed the role-play.

The learning outcomes of both sessions at the level of 2nd year MBBS were identified at the beginning and were displayed again at the end of each session. Discussion and a question-answer session of the audience and presenters were carried out for further elaboration. Feedback of the sessions and student responses were recorded on a predesigned proforma. This included questions regarding the role-play if it was able to generate interest in the given topics in comparison with the traditional way of teaching clinical scenarios. Students were also asked to comment on the over-use of PowerPoint in the traditional teaching methods. The attitude of students in terms of the session being enjoyable was also recorded and the aspect of peer learning was also explored. The response was graded on the Likert scale. Responses were analysed by using SPSS-19. Chi-square test was applied and a $p<0.05$ was considered statistically significant.

RESULTS

Out of 150 students, 137 students participated in the feedback study out of which 56 (40.88%) were male and 81 (59.12%) were female students. 50.4% of the students considered role-play alone as a useful learning tool and 94.9% agreed that if role-play is combined with a multimedia tool then it is useful for learning ($\chi^2=110.43$, $p<0.001$). How useful or useless the various teaching methodologies were deemed by the students is summarised in Table-1.

A total of 95.9% said that role-play is enjoyable ($\chi^2=114.07$, $p<0.001$) and 97.1% said that it is a good technique to improve communication skills ($\chi^2=121.46$, $p<0.001$). 96.4% of students agreed that it was useful for promoting learning in small groups ($\chi^2=117.73$, $p<0.001$) and 85.4% said that they enjoyed

learning from their peers instead of the teacher (χ^2= 68.67, $p<0.001$). Table-2 summarises the perception of students towards different teaching methodologies.

A majority of students have expressed a positive response towards role play as a teaching methodology in the teaching of clinical scenarios in Physiology (Figure-1 and 2).

Table-1: Usefulness or uselessness of various teaching methodologies as reported by students

Teaching methodology	Frequeny	%	χ^2	p
Power Point alone as a teaching tool				
Useful	47	34.3	13.49	0.001
Useless	90	65.7		
Teacher centered teaching and PowerPoint as a teaching tool				
Useful	108	78.8	45.55	0.001
Useless	29	21.2		
Role-play alone as a teaching tool				
Useful	69	50.4	0.007	0.932
Useless	68	49.6		
Role-play and PowerPoint as a teaching tool				
Useful	130	94.9	110.43	0.001
Useless	7	5.1		

Table-2: Students' perception as enjoyable or boring towards various teaching methodologies

Teaching methodology	Frequency	%	χ^2	p
Attitude towards role-play				
Enjoyable	131	95.9	114.07	0.001
Boring	6	4.4		
Attitude towards traditional lectures				
Enjoyable	22	16.1	63.13	0.001
Boring	115	83.9		
Role-play for improving communication skills				
Useful	133	97.1	121.46	0.001
Useless	4	2.9		
Role-play for small group learning				
Enjoyable	132	96.4	117.73	0.001
Boring	5	3.6		
Learning from peers instead of teachers in role-play				
Enjoyable	117	85.4	68.67	0.001
Boring	20	14.6		
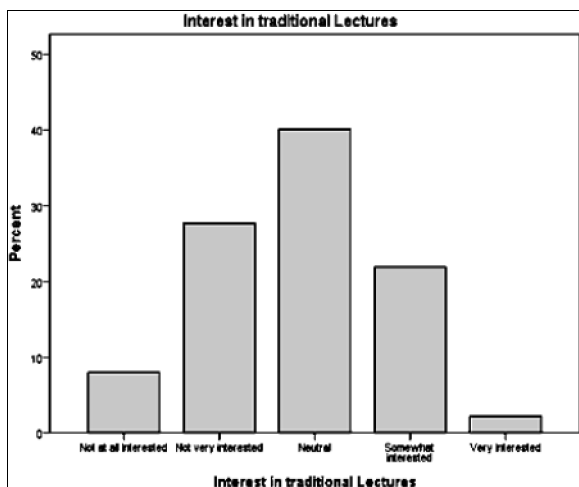
Figure-1: The response of students to traditional lectures in undergraduate Physiology classes
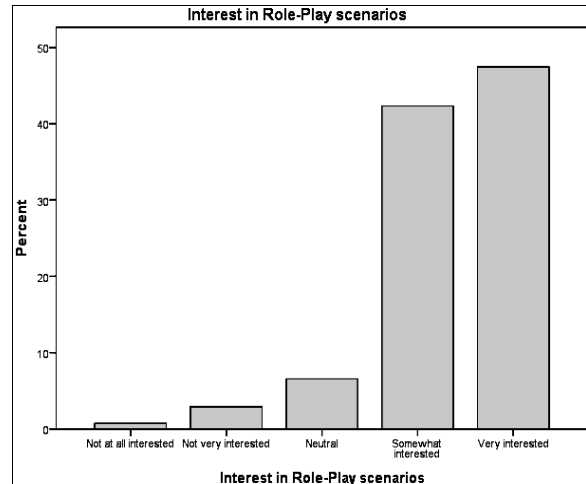
Figure-2: Response of undergraduates towards Role-play in undergraduate Physiology classes

DISCUSSION

Role-play is a type of simulation technique in which people are asked to assume roles and act out exactly as the person would have in a similar situation in real life, often made clear of the objectives needed to be achieved through the given scenario.[21] This technique is used in a wide variety of fields to teach knowledge and skills to the learner. To the best of our knowledge, in CMH Lahore Medical College and Institute of Dentistry, this technique was not previously employed in Physiology classes to teach students physiological concepts and this study was the first of its kind done in the department during an ongoing academic session.

Students in this study found role-play based teaching more enjoyable than traditional lectures; which they recounted as being boring. Role-play was considered a good technique to improve communication skills as reported by 97.1% of the students. These findings are supported by a similar study done in India in which 80% of students said they enjoyed role-playing as a teaching methodology and 90% reported it as being an effective method for learning and improving communication skills.[22]

Our study finding, that 95.9% of the students found role-play an enjoyable teaching methodology, was also supported by a previous study conducted in Chicago USA, in which 85% of the students found the role-play activity enjoyable.[23] Adding to this, our study determined that 50.4% of the students found roleplay a useful teaching technique, this was supported by a study done in South Africa, in which 71% of the students found roleplay a useful technique.[24]

Traditional lectures tend to be more didactic in nature, monotonous, and less engaging while role-play based teaching breaks the monotony, has livelier active class participation, and also helps students to transition easily from these role-play scenarios to

actual cases in the ward while maintaining effective communication skills and increased empathy for real patients. Employing role-play to teach curricula can help students score higher on tests and retain knowledge more as shown in a study done in the USA in which students in the role-play group scored 76% higher after their role-play activity on a post-test.[25]

Various studies explored role-play as a teaching tool in medical education through various research methodologies including pre and post-tests. Our study, however, did not evaluate the students academically to gauge the effectiveness of the technique neither did our study have a large sample size. The learning outcomes of both sessions were assessed by a verbal discussion, and in a large group setting, this discussion was dominated by more vocal students. Thus, the shy students remained away from the limelight.

The actors who volunteered for the role-play scenarios, also spent more time on scripts, props and costumes, and acting, instead of topic discussion, and the question-answer session was mostly tackled by the student who had to present the topic on PowerPoint or Prezi. This study could be further improved on, by future researchers, by using a larger sample size, evaluating the students academically to see a gain in knowledge via pre-test and post-tests, and checking long-term knowledge retention by spaced testing. Also, more sessions may be held on various other topics to involve more students and to present a variety of topics.

CONCLUSION

Role-play not being used as a teaching tool in classrooms is depriving students of an enrichment opportunity, which if planned and executed well by utilizing the resources, could enhance the learning experience of undergraduate medical students in the Physiology classes. The problems associated with role-play lie more in theory than in practice. With careful planning, role-play has the potential to be incorporated in the teaching of clinical scenarios to undergraduate classes to promote learning.

RECOMMENDATIONS

Role-play is an underutilized teaching tool for the demonstration of basic physiological concepts in undergraduate physiology classes. Role-play on its own and in combination with other teaching tools be used in physiology classes to impart knowledge to the students and better prepare them for real-life situations which involve patient management and interaction.

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ORIGINAL ARTICLE
COMPARISON BETWEEN TRADITIONAL, RECORDED, AND ZOOM ONLINE PHYSIOLOGY TEACHING IN UNDERGRADUATE MEDICAL STUDENTS DURING THE COVID-19 PANDEMIC

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Background: Due to COVID-19 educational institutions remained closed for traditional teaching, and online teaching methods were implemented. The recorded physiology lectures were forwarded to students, and teaching was conducted online. The objective of this study was to compare online, recorded, and face-to-face physiology teaching in undergraduate medical students during COVID-19 pandemic. **Methods:** This cross-sectional study was conducted from April to June 2021 at Jinnah Medical and Dental College, Karachi, Pakistan. The study participants included 84 undergraduate 2nd year medical students. The questionnaire included 21 items regarding zoom online, recorded, and traditional teaching. The students selected the preferred teaching method. The data were presented in terms of percentage for individual items, preference in theory, tutorial, and overall preferred teaching method. **Results:** The medical students believed that presence of teacher (86.9%), asking queries to teacher (87%), giving feedback to teacher (81.2%), and interest in learning (83.8%) were more important elements to consider for traditional teaching. Regarding the recorded lectures, understanding the lecture (51.4%), and studying at own pace (52.7%) were found to have high percentage. In relation to preference of teaching method for theory (73.5%), tutorial (76.9%) overall preferred teaching method (78.2%), majority of the students selected traditional teaching method. **Conclusion:** The majority of undergraduate medical students had a preference for traditional teaching methods in Physiology. Among online teaching during COVID-19 pandemic, the students preferred recorded sessions over zoom online classes.
Keywords: COVID-19, Physiology, Traditional, Online, Teaching, Recording

INTRODUCTION

The COVID-19 emerged as a pandemic in March 2020.[1] Due to the severity and widespread of disease, the healthcare professionals suggested social distancing and lockdown restrictions.[2] During the first wave of COVID-19 pandemic, all educational institutions remained closed for traditional/face to face teaching.[3] The teaching in medical schools is based on traditional teaching. The direct interaction of teachers and students is evident in traditional teaching.[4] As the lockdown restrictions were implemented for an indefinite period, there was a transition of teaching methods changed from traditional to online.[5]

Physiology is one of the basic science subject taught in foundation years of medical sciences.[6] Teaching of Physiology makes students understand and comprehend the normal functions and mechanisms of the human body. The importance of physiology teaching/learning is signified by its application in clinical years.[7] Good understanding of physiological concepts helps in studying pathology and medicine.

After the declaration of COVID-19 as a pandemic, the teaching institutions in Pakistan including the medical universities remained closed from March to September 2020. Like a study from Turkey[8], during this period, the recorded Physiology lectures were forwarded to undergraduate medical students of our Institute. The acceptance of recorded lectures was a big challenge for faculty as well as students[5], but it became a necessity to acclimatize to this change in teaching mode due to prolonged closure of educational institutions.

Studies have been published regarding the challenges of online teaching, the advantages and disadvantages of online teaching, and students' perception of online teaching in general. In this study, data were collected from undergraduate students regarding comparison of traditional, Zoom online and recorded Physiology teaching, and preferred teaching method.

METHODOLOGY

The study design was cross-sectional. This study was conducted at Jinnah Medical and Dental College, Karachi, Pakistan for a period of 3 months from April to June 2021. The study participants included 78 undergraduate medical students of 2nd Year MBBS. The sample size was calculated with Raososoft sample size calculator. There were 106 students studying in 2nd year MBBS at Jinnah Medical and Dental College. The sample size was calculated keeping 106 population size, 5% margin of error, 95% confidence interval, and 50% response distribution. The minimum recommended sample size was calculated to be 84.

The study was approved by the Ethics Review Board of Jinnah Medical and Dental College. Informed consent was obtained from all participants. A questionnaire was distributed to all participants and their responses were analysed.

The questionnaire used in our study was developed by Vala et al[4], in which evaluation of e-learning classes in medical students during the COVID-19 pandemic was studied. The questionnaire was modified. Some questions were added and some were removed. Some questions were added in the section of the 'Yes' and 'No' section. The study done by Vala et al[4] compared traditional, e-learning, or both. We compared zoom online, recorded sessions and traditional teaching. The questionnaire containing 21 items was distributed to medical students. The students were asked to select a response for each item on the questionnaire. The undergraduate medical students provided their opinion in individual items. They also selected a preferred teaching method for theory, tutorial and also the overall preferred teaching method.

The data were analysed using SPSS-22. Descriptive statistics were used for the analysis of data. Results were expressed in terms of percentage for each item, for preference in theory, tutorial and the overall preferred teaching method.

RESULTS

The comparison of individual items 1 to 6 is shown in Figure-1. The X-axis shows the item numbers of questionnaire and the Y-axis shows percentage of individual items that students selected in 'Yes' and 'No' format. In majority of items, the students selected the 'Yes' response.

Comparison of individual items 7 to 18 on the basis of preference of traditional, zoom online or recorded teaching methods is shown in Figure-2. The X-axis shows the item numbers and the Y-axis shows the percentage of individual items that students selected for their preferred teaching method. In 9 out of 12 items in this section, the students preferred the traditional teaching method. The individual items include concentration in the class, motivation, asking queries from the teacher, giving immediate feedback to the teacher, feeling more personalized, freedom in learning, collecting the study material, interest in learning, and retention of information for subsequent assessment.

Figure-3 shows comparison of preferred teaching method in theory, tutorial, and overall teaching method. It shows the percentage of preference of teaching method for theory, tutorial and overall teaching method. The majority of students preferred the traditional teaching method.
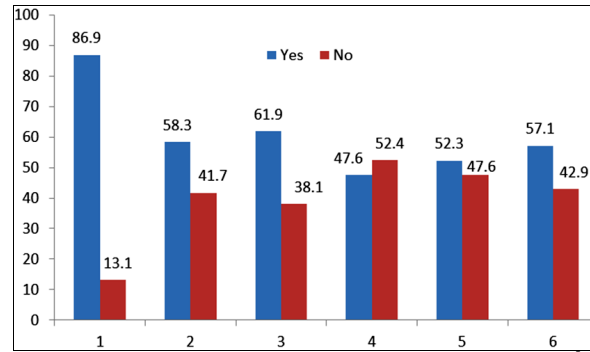
Figure-1: Comparison of individual items 1–6 in 2nd Year MBBS students
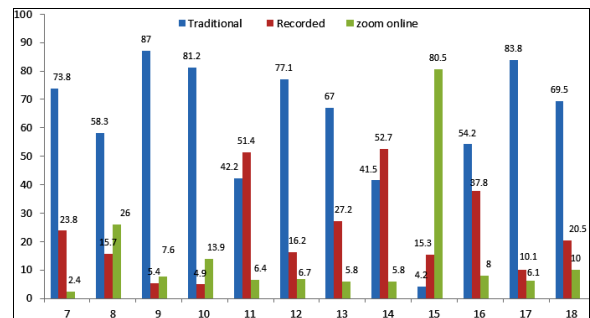
Figure-2: Comparison of items 7–18 on the basis of traditional, recorded, and Zoom online teaching methods in 2nd Year MBBS students
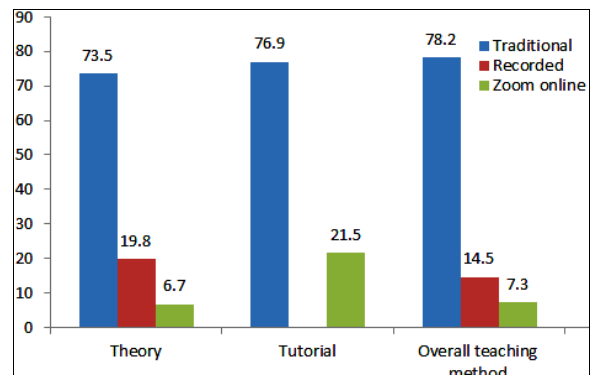
Figure-3: Preference of teaching method in theory, tutorials, and overall teaching methods in 2nd Year MBBS students

DISCUSSION

In 2021, the new session in medical universities in Pakistan started on 1st March. Due to continuation of COVID-19, the Higher Education Commission announced that 50% of the students are allowed to attend classes on campus and the remaining 50% to take online classes. This rule was followed by Jinnah Medical and Dental College where half of the class was attending physically on campus, while the other half attended the lectures live on Zoom.

In this study, comparison between Zoom online, recorded sessions, and traditional teaching

methods was done in 2nd Year medical students during COVID-19 pandemic. Majority of the students selected 'Yes' option for items 1, 2, 3, 5, and 6. Item 1 was related to presence of teacher for learning Physiology. The majority of students were in favour of it. Item 2 was related to students learning affected by presence of colleagues. Item 3 was linked with accessibility of the internet hinders online classes. Item 4 was regarding the internet accessibility hindering the online assessment. Item 5 was related to alignment of online teaching with online assessment. In item 6 the students preferred the optical mark recognition system. In item 1 and 2, our study results were similar to that of Vala[4] et al. In item 3, our students selected the option 'Yes' while in the study of Vala et al.[4] students' selected 'No'. The items 4, 5, and 6 in questionnaire were added in our study.

In the present study, item 7 and 8 of the questionnaire were regarding the concentration and motivation in learning respectively. Item 9 was regarding asking the queries to the teacher, and item 10 was related to giving immediate feedback to the teacher. Item 11 was related to understanding the lecture. Item 12 was linked with the teaching method making students feel more personalized, and item 13 was related to teaching method giving more freedom in learning process. Item 14 was related to the teaching method that helped students to study at their own pace. Item 15 was linked with teaching method by which students get more distracted. Item 16 was linked with the collection of study material. Item 17 was related to interest in learning, and item 18 was regarding the retention of knowledge for assessment. The students selected traditional teaching in items 7, 8, 9, 10, 12, 13, 16, 17, and 18. Abbasi et al[9] and Hameed et al[10] reported that students did not prefer e-learning over face-to-face teaching. Hameed et al[10] recommended blended learning for medical education in future. The study done by Ansar et al[11] mentioned the students' dissatisfaction with e-learning. In our study, students reported the Zoom online classes causing distraction. As suggested by study of Baczek et al[3], to conduct online classes, a well-planned and active approach is required. Our observations in item numbers 7, 8, 9, 10, 11, 14, 15, 17, and 18 were similar to the study done by Vala et al[4]. The students in our study preferred traditional while the students inVala[4] et al study preferred online teaching method for the item 16.

In our study, very small percentage of students selected Zoom online classes. The study done by Alves et al[12] reported that the online classes are difficult to administer in Physiology as many concepts need face-to-face interaction for better understanding. Students also mentioned that the conducive learning environment was lacking at home and internet connectivity was also a big issue. To conduct online classes successfully, an excellent knowledge of the subject, proficient computer knowledge and command, good communication skills, and clarity of expression is required.

Majority of our students liked the Traditional teaching method for theory classes, and tutorials; and the overall preferred teaching method was Traditional. Our results are same as the study done by Vala et al[4] but the percentage of students selecting traditional (73.1%) for theory, (76.9%) for tutorial, and (76.9%) for the overall preferred teaching method was much higher in our study as compared to Vala et al[4] study where 40.8% students selected traditional for theory classes, 51.2% for tutorials, and 59% as the overall preferred teaching method. Our study results are similar to the study by Qamar et al.[13]

CONCLUSION

Majority of undergraduate medical students preferred traditional teaching methods for Physiology. Among online teaching modes, the students preferred recorded sessions over Zoom online classes.

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ORIGINAL ARTICLE

ASSESSMENT OF STRESS, ANXIETY & DEPRESSION LEVELS AMONG MEDICAL FACULTY DUE TO ONLINE TEACHING IN COVID-19

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Background: COVID-19 pandemic brought with it new challenges for teaching activities of the faculty, including need to master the basic use of technology to teach online in changed working environment while dealing with the additional health, family, and work-related challenges. This study aims to evaluate the occurrence of psychological parameters of stress, anxiety, and depression among the participants and the factors for coping with the said psychological parameters. **Methods:** This cross-sectional, questionnaire-based study was conducted in Jan–Jul 2021. Faculty teaching online classes in different medical colleges of Pakistan were invited through social media platforms to participate in the study. The DASS-21 scale was used to evaluate depression, anxiety and stress. **Results:** The factors that had significant contribution to stress, anxiety and depression in the faculty of medical colleges teaching include abrupt transition from face to face to online teaching, job insecurity, and personal and family financial situation. Lack of prior training in proper use of technology was associated with depression, while the uncertainty for duration of the lockdown and personal health issues were associated with anxiety. Coping factor that showed significant association with stress, anxiety and depression was increased intake of drugs. **Conclusion:** There are substantial changes in faculty's mental state concerning exhaustion, stress, depression, and anxiety after switching to online teaching as a result of COVID-19 quarantine. Appropriate measures need to be taken for training of the faculty with IT support, and to ensure peace of mind for the faculty for maximum output.
Keywords: Online teaching, medical colleges, medical faculty, depression, anxiety, stress

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INTRODUCTION

The outbreak of the COVID-19 pandemic was accompanied by drastic changes in organizations all over the world.[1] Lockdowns were implemented globally with educational institutions witnessing a shift from face-to-face to online teaching.[2] Medical colleges went through similar changes, with a complete closure of all clinical activities, with all forms of teaching being shifted to virtual formats. This led to innovations in online teaching in medical education.[2,3]

In order to ensure the quality of the content imparted to medical students, the medical faculty were required to use methods that would improve their engagement with the students.[4] Loss of social contact between the students and teachers during this pandemic has been reported to have a psychological impact on those involved in higher education. During this pandemic, medical teachers have had to learn the use of digital tools with which they were not familiar.[5] Moreover, they have to use different strategies to keep the students engaged during online teaching sessions. Working from home and the lockdown itself have been additional factors that have contributed towards increased levels of stress, anxiety and depression within the medical teaching faculty.[6] Factors like insufficient time to adapt to the sudden changes in teaching dynamics unfamiliarity with technological mode of education, disruptions caused by internet connectivity issues (malfunction). Similarly, difficulty engaging students, job dissatisfaction, and less than optimal work environment are thought to be the main contributors to the decline in mental, social and emotional health of medical faculty.[7]

There is no reported literature describing the levels of stress, anxiety and depression during the COVID-19 pandemic among the medical teaching faculty in Pakistan. The current study aimed to evaluate the levels of stress, anxiety and depression among the medical teaching faculty. A secondary aim of the study was to assess the associated factors with these conditions.

MATERIAL AND METHODS

This was across-sectional, questionnaire-based study conducted from January to June 2021 following Covid-19 lock down in Pakistan. Medical teaching faculty from different medical colleges of Pakistan who were engaged in online teaching were invited to participate in the study. Invitations were sent out through social media platforms, such as Facebook and WhatsApp. Variables were added to Google Forms which comprised of three sections A, B, and C and participants were invited to fill out the forms online.

Stress levels were assessed by employing the Depression Anxiety and Stress Scale-21 (DASS 21).[1,8]

The DASS-21 was added into Section A. This tool consists of 21 items having four options to respond (from 0= did not occur to 3= occurred a lot or most of the time). The items were categorized into three features: depression, anxiety and stress: depression (items: 3, 5, 10, 13, 16, 17 and 21), anxiety (items: 2, 4, 7, 9, 15, 19 and 20) and stress (items: 1, 6, 8, 11, 12, 14 and 18). The scores for the items of each category were added and multiplied by 2 to get separate depression, anxiety and stress scores. These scores were then divided into the following categories: depression (normal 0–9, mild 10–13, moderate 14–20, severe 21–27 and extremely severe 28+); anxiety (normal 0–7, mild 8–9, moderate 10–14, severe 15–19, extremely severe 20+) and stress (normal 0–14, mild 15–18, moderate 19–25, severe 26–33, extremely severe 34+).

In section B, the possible contributors to stress due to online teaching in COVID-19, the participants were asked to rate a list of possible contributors on a 5-point scale, ranging from 0= 'Strongly disagree' to 5= 'Strongly agree' were added. These variables included sudden closure of institutes, connectivity issues, transition from face to face to online teaching, lack of prior training, job insecurity, uncertain duration of lock down, personal and family financial situation, health issues, institutional support, and relocation. We also tried to find out the use of managing strategies during the COVID-19 crisis under the headings, adaptive and maladaptive strategies. The response was documented dichotomously as yes or no to either engaging in positive or negative coping mechanisms Adaptive strategies encompassed exercise, taking healthy food and social digitalizing while maladaptive strategies enclosed behaviours such as excessive smoking, unnecessary drug intake, indulgence to social media.

Section C, included demographic data i.e., age, gender, designation, job description, family support system, number of children and status of spouse.

All the entered data was exported into an Excel file. The data was then exported into SPSS-25. Frequencies and percentages were described for categorical variables such as categories of depression, anxiety and stress; age, gender, designation, job type, family system, number of kids and status of spouse. Mean and standard deviation were described for numerical variables, such as depression, stress and anxiety scores.

RESULTS

A total of 120 medical faculty working in different medical colleges of Pakistan participated in this study. Out of 120, 35 (29.2%) were male and 85 (70.8%) were female faculty members. Most of the participants 48 (40%) were in 36–45 years age group or and rest above 46 years of age 41 (34.2%). The majority of the faculty members were at the position of Assistant Professor 67

(55.8%). Moreover, our sample included most of the participants from private institutions 98 (81.7%). All patient characteristics have been illustrated in Table-1.

Table-1: Medical faculty characteristics (n=120)

Characteristic		Frequency (%)
Age	25–35 Years	31 (25.8%)
	36–45 Years	48 (40%)
	≥46 Years	41 (34.2%)
Gender	Male	35 (29.2%)
	Female	85 (70.8%)
Designation	Assistant Professor	67 (55.8%)
	Associate Professor	24 (20%)
	Professor	29 (24.2%)
Job Description	Government	22 (18.3%)
	Private	98 (81.7%)
Family Support System	Nucleus	70 (58.3%)
	Joint	50 (41.7%)
Number of Children	1	28 (23.3%)
	2	39 (32.5%)
	3	32 (26.7%)
	>3	21 (17.5%)
Spouse Working	Working	76 (63.3%)
	Not Working	29 (24.2%)
	No spouse	15 (12.5%)

Faculty were asked to rate their level of depression, anxiety and stress with regard to teaching online during the current COVID-19 pandemic. The frequency rates of depression, anxiety and stress were found to be 36 (30%), 42 (35.3%) and 31 (25.8%). The relationship of stress, anxiety and depression with different contributing factors has been illustrated in Table-2. Abrupt transition to online teaching, job insecurity, personal financial situation and family financial situation were found to be significant contributing factors associated with stress, anxiety and depression.

The relationship of different coping factors with stress, anxiety and depression have been shown in Table-3. Crosstab followed by chi square test was applied to calculate percentages and *p*-value. No participant reported to either start smoking or increasing smoking during the COVID-19 pandemic. The only coping mechanism found to have a significant association with stress, anxiety and depression was increase in the use of drugs, as shown in Table-3.

Out of a list of 11 possible contributors, 8 were found to be statistically significant. One of the possible contributors was internet issues leading to anxiety (0.020). Abrupt transition to online teaching led to depression (0.006), anxiety (0.001), and stress (0.031). Lack of prior training lead only to depression (0.004). Another cause of depression (0.001), anxiety (0.001) and stress (0.045) were job insecurity. Uncertain duration of lock-down was found to cause only anxiety (0.001). Personal and family financial situation contributed to depression (0.003, 0.012), anxiety (0.002, 0.002), and stress (0.045, 0.001) respectively. Personal health issues caused anxiety (0.041).

Table-2: Relationship of depression, anxiety and stress with different contributing factors

Parameter		Depression			Anxiety			Stress		
		Normal	Depression	p	Normal	Anxiety	p	Normal	Stress	p
Sudden closure	Agree	63.1%	66.7%	0.708	61.0%	69.0%	0.385	61.8%	71.0%	0.359
	Disagree	36.9%	33.3%		39.0%	31.0%		38.2%	29.0%	
Internet issues	Agree	82.1%	91.7%	0.181	79.2%	95.2%	0.020*	84.3%	87.1%	0.704
	Disagree	17.9%	8.3%		20.8%	4.8%		15.7%	12.9%	
Abrupt transition to online teaching	Agree	60.7%	86.1%	0.006*	57.1%	88.1%	0.001*	62.9%	83.9%	0.031*
	Disagree	39.3%	13.9%		42.9%	11.9%		37.1%	16.1%	
Lack of prior training	Agree	56.0%	83.3%	0.004*	58.4%	73.8%	0.095	60.7%	74.2%	0.176
	Disagree	44.0%	16.7%		41.6%	26.2%		39.3%	25.8%	
Job insecurity	Agree	21.4%	52.8%	0.001*	19.5%	50.0%	0.001*	25.8%	45.2%	0.045*
	Disagree	78.6%	47.2%		80.5%	50.0%		74.2%	54.8%	
Uncertain duration of lock down	Agree	91.7%	100.0%	0.074	19.5%	50.0%	0.001*	92.1%	100%	0.108
	Disagree	8.3%	0%		80.5%	50.0%		7.9%	0%	
Personal financial situation	Agree	22.6%	50.0%	0.003*	23.4%	45.2%	0.002*	25.8%	45.2%	0.045*
	Disagree	77.4%	50.0%		76.6%	54.8%		74.2%	54.8%	
Family financial situation	Agree	15.5%	36.1%	0.012*	13.0%	38.1%	0.002*	14.6%	41.9%	0.001*
	Disagree	84.5%	63.9%		87.0&	61.9%		85.4%	58.1%	
Personal health issues	Agree	41.7%	50.0%	0.400	37.7%	57.1%	0.041*	39.3%	58.1%	0.070
	Disagree	58.3%	50.0%		62.3%	42.9%		60.7%	41.9%	
Institutional support	Agree	53.6%	44.4%	0.359	53.2%	47.6%	0.557	52.8%	45.2%	0.463
	Disagree	46.4%	55.6%		46.8%	52.4%		47.2%	54.8%	
Relocation	Agree	14.3%	23.8%	0.193	14.3%	23.8%	0.193	14.6%	29.0%	0.074
	Disagree	85.7%	76.2%		85.7%	76.2%		85.4%	71.0%	

*Significant

Table-3: Relationship of different coping factors with depression, anxiety and stress [n (%)]

Parameter		Depression			Anxiety			Stress		
		Normal	Depression	p	Normal	Anxiety	p	Normal	Stress	p
Exercise	Agree	36 (42.9)	14 (38.9)	0.686	32 (41.6)	18 (42.9)	0.891	39 (43.8)	11 (35.5)	0.417
	Disagree	48 (57.1)	22 (61.1)		45 (58.4)	24 (57.1)		50 (56.2)	20 (64.5)	
Healthy eating	Agree	67 (79.8)	27 (75.0)	0.562	59 (76.6)	34 (81.0)	0.585	71 (79.8)	23 (74.2)	0.516
	Disagree	17 (20.2)	9 (25.0)		18 (23.4)	8 (19.0)		18 (20.2)	8 (25.8)	
Digital socializing	Agree	64 (76.2)	28 (77.8)	0.851	56 (72.7)	35 (83.3)	0.192	69 (77.5)	23 (74.2)	0.705
	Disagree	20 (23.8)	8 (22.2)		21 (27.3)	7 (16.7)		20 (22.5)	8 (25.8)	
Increased drug use	Agree	0 (0)	4 (11.1)	0.002*	0 (0)	4 (9.5)	0.006*	1 (1.1)	3 (9.7)	0.022*
	Disagree	84 (100.0)	32 (88.9)		77 (100.0)	38 (90.5)		88 (98.9)	28 (90.3)	
Adoption of new hobbies	Agree	44 (52.4)	17 (47.2)	0.604	38 (49.4)	23 (54.8)	0.573	41 (46.1)	20 (64.5)	0.077
	Disagree	40 (47.6)	19 (52.8)		39 (50.6)	19 (45.2)		48 (53.9)	11 (35.5)	

*Significant

DISCUSSION

The present study was done to assess the levels of stress, anxiety and depression among medical faculty members during the COVID-19 pandemic and evaluate the relationship of these psychological parameters with various contributing factors and coping mechanisms.

The majority of the participants in our sample were females 85 (70.8%). Although the specialty of the participants was not recorded, the principal investigator did observe that the majority of the participants were from basic medical sciences. In Pakistan, the majority of the faculty members in basic medical sciences are generally females. Moreover, since the investigators approached more private medical colleges, there was a significantly greater number of participants from private medical colleges 98 (81.7%).

With respect to the other socio-personal parameters, those with children showed more anxiety than those without, all though the difference is not significant. Furthermore, faculty members who suffered with chronic diseases and those who lived with a person having some chronic illness exhibit a significantly higher level of anxiety. Additionally, those who lived with a person who has been infected with COVID-19 also showed greater levels of anxiety, possibly due to the fear of infecting the ill relative, along with the fear of being infected themselves.[9]

Our study found that the abrupt transition to online teaching was significantly associated with stress, anxiety and depression. This implies that since the medical teachers were not prepared for online teaching, this transition was quite difficult for them. They were not able to cope with different mode of teaching and the associated technology use. Online teaching requires using digital gadgets and being well-versed with the software used for teaching. Not knowing how to use these gadgets and software meant that the teachers had to first learn how to use these tools and then use them for teaching their students. Lack of prior training and not being comfortable with the relatively newer modes of teaching led to an increase in the occurrence stress, anxiety and depression among the faculty.[10] This led to a feeling of job insecurity among professionals. The medical teaching profession was similarly affected by this job insecurity phenomenon. The findings of our study substantiate this point as suggested by the significant association found between job insecurity and the occurrence of stress, anxiety and depression.

The results of our study are consistent with the study carried out by Rasmitadila, *et al*, which emphasised that majority of the teachers were found to be in moderate perceived stress pertaining to job insecurity during the uncertain period of Covid.[11]

The pandemic had serious economic implications all over the world. Our study found that both personal and family financial situations were associated with psychological parameters, as shown in Table-2. Salary cuts were commonly observed during the pandemic and along with job insecurity, this had serious psychological implications for medical teachers. Study conducted by Haleem, *et al*, concluded same results with emphasis on psychological and financial impacts of COVID-19 on medical educators.[12]

The only coping mechanism found to be significantly associated with the stress, anxiety and depression was the increased use of drugs. Although a statistical difference was observed between medical teachers who were having psychological effects and those who were not but the frequency differences were apparently not of a significant value. For instance, only four (11.1%) of the depressed teachers increased drug usage as compared to none (0%) of those who were not depressed. Similar differences were seen for anxiety and stress as well. Although the differences are small, the significant difference must be addressed with caution since increasing use of drugs among medical teachers is an alarming finding. The results are supported by study conducted by Austin V, *et al.*[13]

CONCLUSION

This study discovered substantial changes in faculty's mental state concerning exhaustion, stress, depression, and anxiety after switching to online teaching as a result of COVID-19 quarantine.

RECOMMENDATIONS

There is a need for proper training of the medical teaching faculty in different medical colleges of Pakistan for online teaching. Appropriate measures need to be taken to ensure job security for peace of mind for the faculty for maximum output. Further studies should contact clinical teachers as well as faculty members from more government colleges. IT support needs improvement.

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ORIGINAL ARTICLE
KNOWLEDGE OF BEDSIDE ETHICS AND ITS IMPLEMENTATION IN A PUBLIC SECTOR UNIVERSITY HOSPITAL

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Background: Medical ethics have always been considered as fundamentally important and bedside ethics are challenging to teach due to lack of formal teaching sessions. This study aimed to identify the knowledge, attitude and misconceptions among medical students about bedside ethics in hospital and its implementation in their routine practice. **Methods:** The cross-sectional study was conducted in medical students from 3rd, 4th, and 5th year from public sector medical colleges from June to August 2020. **Results:** Out of 400 Medical students, 90% had knowledge about bedside ethics and 64% knew the principle of bedside ethics. Sixty-four of medical students believed that they lived in an environment that was inappropriate for an ethical evaluation of the doctor-patient relation. Three-hundred-forty-one (84%) opted to recognize the patient and address them in a sophisticated reserved manner when approaching the patient at bedside. Two-hundred eleven (52%) preferred to inform bad news to patients in front of their attendants. Two-hundred ninety-eight (73%) of medical students believed that ethics were required for moral values. Three-hundred-five (75%) selected the option to tell the patients honestly when they make a mistake while treatment. Moreover, 259 (64%) of students preferred to ask patients to expose the target body part but 131 (32%) of students preferred to do it by themselves. **Conclusion:** Majority of the undergraduate medical students had knowledge about bedside ethics and its principle. Inculcation of ethics as a subject into the curriculum of MBBS students is suggested.

Keywords: Knowledge, bedside ethics, implementation, public sector, medical students

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INTRODUCTION

Medical ethics refers to a system of moral guidelines that apply value and judgment to the practice of medicine.[1] Ethics has always been of fundamental importance to the medical profession[2], and with the advancement in the field of medicine, the significance of medical ethics has grown many folds[3]. Special emphasis is given to incorporate it in the training of medical students around the world, and it is taught as a component of Behavioural Sciences —a mandatory part of undergraduate medical school teaching.[4] Teaching bedside manners proves to be one of the most challenging tasks in medical education, since it is difficult to organize formal training sessions in this domain.[5] Practices differ across the countries based on their norms and values leading to disparity in the knowledge being conveyed to health care providers. World Health Organization (WHO) has developed a comprehensive teaching module on ethics to cater to the needs of medical students based on their region-specific practices.[6]

In Pakistan, lack of a structured curriculum for ethics in medical education has resulted in health care professionals being inadequately trained in medical ethics. Though, the current MBBS curriculum prepared by Pakistan Medical and Dental Council (PMDC) provides objectives and course outline for teaching ethics[7], but it lacks details of implementation. Unlike other countries, in Pakistan the components of Medical Ethics are incorporated into the Forensic and Community Medicine curricula instead of being taught as a separate subject.[8] Medical curriculum in Pakistan fails to effectively address the ethical issues faced by a doctor.

Medical students interact with patients in their clinical rotations and will soon become primary care practitioners encountering more patients in future. It is imperative to have the necessary knowledge regarding medical ethics, as well as the right attitude to follow the ethical code. This study aimed to identify the knowledge, attitude and misconceptions among medical students about bedside ethics in hospital and its implementation in their routine practice.

MATERIAL AND METHODS

This cross-sectional study was conducted over a period of 3 months from June to August 2020. A sample size of 400 was estimated with a 95% confidence interval using OpenEpi. Ethical approval for the survey was taken from the Ethical Review Board. Volunteers included medical students from 3rd, 4th, and 5th year from public sector medical colleges. Medical students in the private sector were excluded.

A self-administered questionnaire was designed with the help of experts from the Department of Medical education and Psychiatry to

collect the data for the survey. The questionnaire consisted of 18 multiple-choice-questions which tested a students' ethical knowledge and its implementation in clinical settings with pilot study. The volunteers received no prior notification of the study. It was voluntary to fill the questionnaire and the volunteers were reassured that their responses will be kept confidential and 80% response rate was received.

Data were analysed using SPSS-16. Descriptive analysis was done with frequencies and percentages for all data including the comparison of attitudes towards practical ethical problems among students and patients.

RESULTS

Four-hundred-eight medical students participated in this study and responded to a self-administered questionnaire of 18 ethic-based inquiries. The 90% of medical students had Knowledge about bedside ethics and 64% knew the principle of bedside ethics. The 64% of medical students believed that they lived in an environment that was inappropriate for an ethical evaluation of the doctor-patient relation (Table-1).

Three-hundred-forty-one (84%) Opted to Recognize the patient and address them in a sophisticated reserved manner when approaching the patient at bedside (Figure-1). Two-hundred-elevon (52%) preferred to inform bad news to patients in front of their attendants (Figure-2). Two-hundred-nintyeight (73%) of medical students believed that ethics were required for moral values (Figure-3).

Three-hundred-five (75%) selected the option to tell the patients honestly when they make a mistake while treatment, 19 (5%) selected denial making a mistake, 14 (3%) selected to lie to the patient to save another colleague and only 7 (2%) opted to blame it on staff or another colleague.

Responding to the question that when patients refused treatment based on religious grounds, most of the students 330 (81%) chose to counsel the patient, 33 (8%) chose to let them go without treatment and 15 (4%) chose not to listen to the patient and continue the treatment.

Almost half of the participants believed that age above 18 years was appropriate for consent writing and only 71 (17%) believed that patient of any age was fit to give consent. Meanwhile, most of the students 376 (92%) preferred to stand on the right side of the patient while treatments and history taking, and 364 (90%) opted to take permission every time for treatment. Moreover, 259 (64%) of students preferred to ask patients to expose the target body part but 131 (32%) of students preferred to do it by themselves.

Table-1: Medical students' knowledge and attitude of ethics toward their patients

|	Yes n (%)	No n (%)
Do you have any knowledge about bedside ethics?	366 (90)	42 (10)
Was the subject of bedside ethic were specifically discussed?	217 (53)	191 (47)
Do you know about the principles of bedside ethics?	261 (64)	147 (36)
Did you ever get evaluated based on your ethical attitude?	190 (47)	218 (53)
Do you as a patient think that ethical protocols are being practiced among the physician on the bedside?	172 (42)	236 (58)
Do you think the environment you live in is appropriate for an ethical evaluation of the doctor-patient relation?	147 (36)	261 (64)
Do you introduce yourself to the patient/attendant?	398 (97.5)	10 (2.5)
Call your patient with their name?	278 (68)	130 (32)
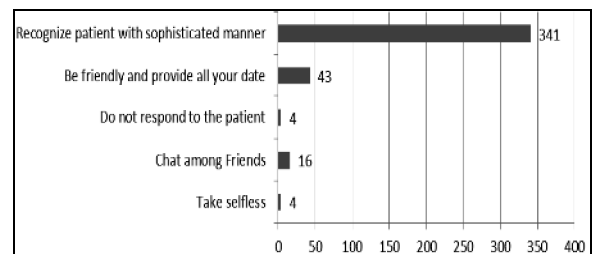
Figure-1: Medical students' attitude toward their patient at bedside
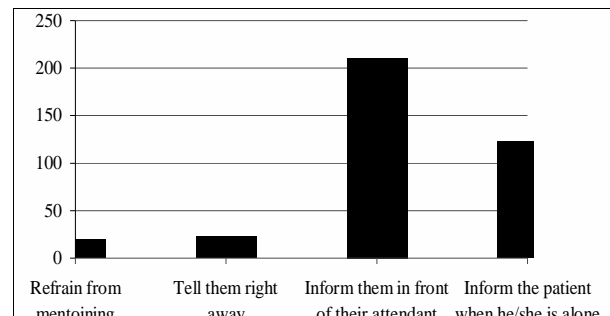

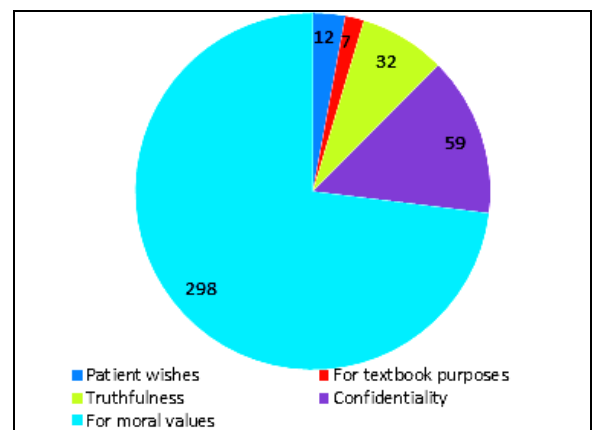**Figure-2: Medical students' attitude to deal with bad news**

Figure-3: Medical students' attitude about ethics

DISCUSSION

Our study evaluated 3rd year, 4th year, and final year medical students about their knowledge and attitude related to medical ethics in colleges affiliated with public sector medical university in Karachi.

One component of our study was to understand the knowledge of ethics among medical students. Results of our study showed that the majority of medical students (90%) knew bedside ethics. These results were similar to cross-sectional studies conducted by Chatterjee and Sarkar[9] in Bangladesh and another study by Walrond et al[10] from Barbados. However, in the cross-sectional survey from Pakistan, Majeed et al[11], reported that most of the students were not aware of medical ethics. It was observed that third-year MBBS students had more knowledge than fourth and final year students since behavioural sciences were incorporated as a subject into the third year curriculum while fourth and final year students had a curriculum focused on clinical subjects. The finding of this study is in contrast to the findings of our study and the plausible explanation for this contrast between the two studies may be the incorporation of ethics into the modular curriculum of sciences in the third, fourth, and final year, at public sector setting of healthcare training, which may have resulted in better understanding of ethics.

Beauchamp and Childress introduced four principles of ethics including autonomy, beneficence, non-maleficence, and justice.[12] These four principles along with the right to refuse treatment, Fairness or equity, Capacity, or competence are essential in understanding the modern concepts of ethics.[13] In a recent cross-sectional survey from Malaysia[14], it was observed that only 18% of the MBBS student knew the basic principles of ethics. Similar findings were reported in a cross-sectional survey from Azad Kashmir[15], Pakistan, the majority of students did not know about the basic principles of ethics. Surprisingly, more than half (64%) of students knew about basic principles of ethics in our study; a possible reason for this finding could be the inculcation of basic principles of ethics in the curriculum of the third, fourth and final year MBBS program in our study. At present ethics is incorporated into the subject of forensic medicine and community medicine and is not taught as a separate subject in the majority of medical colleges across Pakistan and these observations highlight the need to introduce ethics as a separate subject in the medical curriculum of MBBS.[8]

Another component of our study was to understand the attitude of medical students towards the patients. It was observed that more than half 55% of students preferred to inform bad news to patients in front of their attendants. These findings are similar to the observations in a cross-sectional study on final year medical students Iswarya and Bhuvaneshwari[16] where 61% of participants agreed that close relatives of patients always were informed about the patient's condition. Likewise in cross-sectional studies by Subramanian et al[17] and Borgen et al[18] on physicians, similar findings were reported. Similarities of findings reported by the authors of South Asian countries reflected common values and beliefs shared by the population of this region.

Medical errors may be defined as accidental harm to patient harm caused by health care providers and may have serious consequences on a patient's health and well-being and it is estimated that 50% to 96% of errors go unreported in the healthcare delivery system.[19] In this study, more than half (75%) opted to tell the patients honestly when they made a mistake during treatment, 5% opted to deny, 3% chose to lie to the patient to save a friend while 2% selected the option to blame it on staff or another medical student. This is in accordance with the findings of studies conducted earlier on this subject, where the majority of students chose to inform the patient about the mistake made by a doctor.[16,20,21] On the other hand, a cross-sectional survey on residents of the faculty of medicine by Mohammed et al[22] discovered that 83% of residents disagreed that patients should always be informed about the mistake made by health workers, and mentioned fear of malpractice as their key reason for disagreement.

According to our study, almost half of the participants believed that age above 18 years was appropriate for giving consent and 73% believed that not every patient is fit to giving consent. Similarly, Chatterjee and Sarkar[9] observed that many participants had agreed that children should never be treated without the consent of their parents.

Observations of our study have to be interpreted after considering the limitations of this study. This strength of this study were large sample size and sample population covering different institutes of a public sector university, however, findings were based on self-reported knowledge, what students believed. Moreover, this survey does not compare the responses between third, fourth, and final year survey, and a comparative study would have given a holistic picture of understanding of knowledge and attitudes of students as they progress from to the final year, exposed to the clinical situations demanding ethical consideration.

CONCLUSION

Majority of the undergraduate medical students had knowledge about bedside ethics and its principle. Inculcation of ethics as a subject into the curriculum of MBBS students is suggested.

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ORIGINAL ARTICLE
IMPACT OF LOCKDOWN DUE TO CORONAVIRUS DISEASE (COVID-19) ON THE WEIGHT RELATED QUALITY OF LIFE

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Background: The current lockdown due to the COVID-19 pandemic has clearly led to changes in the lifestyles of people. This study aimed to determine the effects of this lockdown on the lifestyles of individuals and ultimately the overall changes in weight-based quality of life in the undergraduate students of Pakistan. **Methods:** This cross-sectional study was conducted on participants of ages 18–25 from different universities around Pakistan. The questionnaires were sent to participants via WhatsApp, posted online using Microsoft forms. A total of 157 responses were received. The questionnaires were adapted using Impact of Weight on Quality of Life (IWQOL). Chi-square test was used for comparison of categorical variables, and $p<0.05$ was considered statistically significant. **Results:** Out of 157 responses, 109 were females and 48 males. The mean weight before and after the lockdown was 61.95 Kg and 64.97 Kg respectively. Significant changes in areas of physical function, self-esteem and work were attained with $p<0.001$, 0.002, and 0.023 respectively. **Conclusions:** The lifestyle changed and as a result the weight of the undergraduate population of Pakistan generally increased during the lockdown due to the COVID-19 pandemic. Self-esteem decreased among the youth and they faced mental health issues including anxiety and distress due to direct effects of lockdown on lifestyle.
Keywords: Lockdown, Obesity, Lifestyle, Anxiety, Body image, Stress, Physical function

INTRODUCTION

As countries started to lockdown in March 2020 with the surge in COVID-19 cases, people were forced to spend most of their time indoors. Stress and anxiety among the people increased.[1] The factors that contributed significantly to this rise include not only the fear of infection but also the long duration of isolation, running out of basic commodities, boredom, frustration due to financial strains and unemployment.[1]

As the uncertainty surrounding the duration of the pandemic increases, people tend to make unhealthier lifestyle choices. People tend to choose foods with a longer shelf life that are highly processed and rich in calories.[2] This not only affects adults but also children. As schools, workplaces, and gyms closed down, opportunities for physical activity also declined. Previous studies have established lower frequency of vigorous physical exercise is significantly associated with higher rates of diagnosed depression.[3] People also have an unhealthier sleeping pattern during holidays.[4] All of these factors, i.e., unhealthy diet, lack of physical activity, and poor sleeping habits cause lower quality of life.[5] A decline in health-related quality of life (HRQOL) has been reported by a study conducted in China with pain/discomfort being the most frequently reported problem followed by anxiety/depression.[6] On the contrary, a study in Vietnam found that HRQOL was better during the pandemic than before.[7] Another study in China found a mild stressful impact of the pandemic with more than half the population reporting

fear but a majority did not feel helpless. It also reported increased support and care from friends and family leading to positive mental health-related lifestyle changes.[8] Ferreira *et al* report higher anxiety and lower HRQOL levels in Portuguese with women and the elderly most prone to the problem.[9]

Since the start of the pandemic, several research articles have come forward demonstrating the effect of the pandemic on mental, emotional, and health-related quality of life worldwide. However, the research on this topic on Pakistani population still seems to be absent. This study analyses weight gain during the pandemic as a direct measure impact of weight on quality of life in a quantitative manner. Previous studies to evaluate the threat of obesity and worsening quality of life post-pandemic have been conducted in UAE, Spain, Croatia, Italy, and Poland.[10–13]

This study aims to find changes in the weight-based quality of life of undergraduates during the lockdown (Mar–Sep 2020) and its impact on physical function, self-esteem, public distress, and work life. It also aims to highlight the problem to promote awareness for adequate measures to reduce the risk for lower perceived quality of life.

METHODOLOGY

Ethical approval was given by the Ethical Committee of CMH Lahore Medical College and Institute of Dentistry (No. 485/ERC/CMHLMC). Participants included both males and females enrolled in different universities of

Pakistan and belonging to the age group of 18–25 years from mid-March 2020 to mid-September 2020. The exclusion criteria included participants younger than 18 years or older than 25 years and those not enrolled in a university of Pakistan. The sample size was calculated to be 157 using the Rao soft formula with 95% confidence interval and 5% margin of error. The population size used was calculated by using values of Zachary *et al.*[5]

Questionnaires were administered online using Microsoft Forms in August and September 2020. The questionnaires were adapted using Impact of Weight on Quality of Life (IWQOL).[14] The questions designed included questions from the areas: physical function, self-esteem, public distress, and work, respectively. Question 1 to 6 collected bio-data of the participants including name, age, gender, university, last measured weight before the lockdown, and weight at the time of filling the questionnaire. Question 7–16 were adapted from the IWQOL. Each question was rated on a three-point Likert scale with 'Never' scoring 0 points, 'Sometimes' scoring 3 points, and 'All the time' scoring 5 points. The scores were additive and higher scores meant a greater impact of weight gain on physical function, self-esteem, public distress, and work.

The data were analysed on SPSS-26 for mean score, and standard deviation of all variables. The highest scores possible were 15, 20, 5 and 5 for physical function, self-esteem, work, and public distress respectively. The lowest score for all variables was 0. The total score was achieved by summing all scores. Results were presented as frequency and percentages. Chi-square test was used for comparison of categorical variables, and $p<0.05$ was taken as significant.

RESULTS

One-thousand people were contacted to fill the survey. Only 162 responses were collected of which 5 were rejected due to incomplete data or not meeting the inclusion criteria, and 157 people who completed the survey were selected. A total of 109 were females and 48 were males. The participants (n=157) were in age group 18–25 years with mean age of 21.2±1.19 years. The mean weight before the lockdown was 61.95±13.8 Kg and after lockdown was 64.97±13.6 Kg, with a mean increase of 3.02 Kg. The average score for part 1 of the survey assessing the quality of life was 12.19±3.24 before lockdown and 12.86±3.89 after the lockdown (Table-1). The increase in this score was not significant.

On breaking down the data into areas of physical function, self-esteem, work, and public distress, a significant impact was seen on physical function, self-esteem, and work but not public distress. The *p* were <0.001, 0.002, 0.023, 0.612 for areas of physical function, self-esteem, work, and public distress respectively (Table-2).

A deeper analysis of the data found physical function declined in two variables relating to moderate exercise. Trouble climbing stairs/running (*p*=0.033) and trouble with stiff joints (*p*=0.002) were the two significant problems faced by the population after lockdown. The area of self-esteem also showed significant differences for fear of being rejected (*p*=0.04) and avoiding looking at oneself in mirror or photographs (*p*=0.033). The differences were significant (*p*=0.02) for the variable concerning the area of work, i.e., trouble getting things accomplished or meeting my responsibilities. The variables for public distress did not prove to have a significant *p*-value (Table-3).

Table-1: Scores and standard deviation for assessment of weight and the quality of life

	Assessment of weight (Kg)	Assessment of quality of life
Average Score	Mean±SD	Mean±SD
Before lockdown	61.95±13.8	12.19±3.24
After lockdown	64.97±13.6	12.86±3.89

Table-2: Scores for areas of physical function, self-esteem, public distress, and work before and after the lockdown in population (Score, Mean±SD)

Parameters	Before lockdown score	After lockdown score	*p*
Physical Function	2.21±2.90	3.00±3.46	0.000
Self Esteem	5.00±5.48	5.89±6.24	0.002
Work	0.42±1.13	0.57±1.36	0.023
Public Distress	1.36±1.66	1.41±1.74	0.612

Table-3: Variables for physical function, self-esteem, public distress, and work before and after the lockdown

	Never		Sometimes		Always		
	Before Lockdown	After Lockdown	Before Lockdown	After Lockdown	Before Lockdown	After Lockdown	*p*
Physical Function							
Because of my weight, I have trouble climbing stairs/running	114	106	38	44	5	7	0.033
I am troubled by painful or stiff joints	105	92	50	60	2	5	0.002
Self-esteem							
Because of my weight, I am afraid of being rejected	116	108	28	29	13	20	0.04
Because of my weight, I avoid looking in mirrors or seeing myself in photographs	118	110	35	39	4	8	0.033
Work							
Because of my weight, I have trouble getting things accomplished or meeting my responsibilities	137	132	17	18	3	7	0.020
Public distress							
Because of my weight, I experience ridicule, teasing or unwanted attention	103	96	38	43	16	18	0.07

DISCUSSION

This cross-sectional study shows the association between weight-based quality of life and lockdown during the Covid-19 pandemic in Pakistan. The quality of life has worsened in the lockdown, owing to lack of physical activity, increased anxiety, poor dietary habits, and lack of peer interactions.[15] Overeating and poor exercise led to socially unacceptable raised body weight leading to a rise in mental health issues.[16] In Pakistan, these issues were not very well addressed. Though there was inauguration of the telemedicine concept, but due to rural-urban disparity, it failed to address these problems.[17]

Low physical activity and lipid deposition in various systems of the body lead to cardiovascular disease, diabetes mellitus, and dyslipidaemia. There is an increase in cytokines release and angiotensin which causes hypertension.[18] There is an increased risk of breast cancer, endometrial cancer, and other cancers.[19–21] It can also affect the immune responses of the body, making it vulnerable to infections and less responsive to vaccinations, anti-virals, and antimicrobial therapies.[22] High BMI can lead to increased levels of inflammatory mediators like TNF, IL-1, IL-6, resulting in osteoarthritis.[23] The problem of osteoarthritis linked with obesity is more commonly seen in women, affecting the larger stabilizing joints mostly like knee, back, and hip, that is important in performing physical activities like climbing stairs.[24] This is homogenous to our findings; a significant number of individuals report trouble with stiff joints after lockdown. People were discouraged to visit their doctor because of ongoing pandemic and routine medical check-ups were ignored. This may lead to health issues in future.

The pandemic had a considerable number of negative effects on the mental health of people. Etxebarria *et al*[25] reported higher levels of stress, depression, and anxiety after the lockdown in Spain. Depression, anxiety, and stress after lockdown order has also been prevalent in the Indian population with recommendations for urgent intervention from the government.[26] The mental health of the Pakistani population has taken a toll downwards as 16 cases of suicide linked to COVID-19 were reported with the most common cause being economic recession and distress followed by fear of infection.[27] More people feared social rejection after lockdown than before lockdown. This led them to avoid looking at themselves in mirrors, i.e., self-avoidance. Other contributory factors include peer victimization, unwanted teasing, and societal pressure.[28] These have also been obvious in the present study.

The limitations of our study include the questionnaires being sent online. There might be a chance that these were not responded by the individuals themselves which may lead to ambiguous results. A proper identification procedure must have been added to avoid such discrepancies. People who might have been the worst affected in terms of weight-related quality of life might not have come forward to fill the survey due to shyness or embarrassment of social stigma. In future studies, a broader spectrum of age groups and a larger sample size should be used to get an accurate idea about how the quality of life altered within individuals, and if possible, the health-related quality of life should be measured to find the future impact of this pandemic on healthcare needs.

CONCLUSION

The COVID-19 pandemic has brought out a lot of problems which not only include unemployment, poverty, mental health problems like anxiety and depression, but also debilitated quality of life and physical health. The community-wide quarantine during the COVID-19 pandemic is causing weight gain and hence lower quality of life in young adults. Young adults have problems with day-to-day physical activities like climbing stairs, and complain of stiff joints. Self-esteem has been adversely impacted. Meeting one's responsibilities has also become difficult which can be attributed to both declining physical health as well as mental health. There is an utmost necessity of finding ways to improve the quality of life in individuals which may block the rise of other associated problems like obesity, depression. Otherwise, we may be heading towards lowered overall quality of health in young people.

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ORIGINAL ARTICLE

PERCEIVED STRESS, EMOTIONAL INTELLIGENCE, COPING STRATEGIES, AND MARITAL ADJUSTMENT IN DUAL EARNER COUPLES

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Background: It has often been experiential that dual earner couples with the passage of time become more frustrated and strict due to lots of burden and that may affect their marital life too. The Present study aimed to investigate the relationship among Perceived Stress, Emotional Intelligence, Coping Strategies and Marital Adjustment in Dual Earner Couples. **Method:** This was a cross sectional study conducted on the sample of 75 dual earner couples (n=150) with the age range of 25–45 was selected by using the Non-Probability Purposive Technique. Data was taken from different Govt. and Private Institutes of Lahore. Perceived Stress Scale (PSS), Schutte Self Report Emotional Intelligence Test (SSEIT), Brief COPE Inventory (BCOPEI) and Revised Dyadic Adjustment Scale (RDAS) were applied on the participants along with demographic questionnaire. Pearson Product Moment Correlation Coefficient, Multiple Regression analysis and Independent Sample *t*-test was used in the study. **Results:** The Results showed that there was a significant negative correlation between Perceived Stress and marital adjustment (*r*= -0.25, *p*=0.001), whereas, Emotional Intelligence (*r*=0.46, *p*=0.000) and Coping Strategies (*r*=0.15, *p*=0.033) have significant positive relationship with Marital Adjustment. Perceived Stress (*p*=0.23) and Coping Strategies (*p*=0.92) are not well predictors; however Emotional Intelligence (*p*=0.000) was found a significant predictor of Marital Adjustment (R^2=0.22). The findings also depicted that there was no gender difference regarding the study variables. **Conclusion:** Perceived stress has negative but emotional intelligence and coping strategies have positive effect on marital adjustment.

Keywords: Perceived stress, Emotional intelligence, Coping strategies, Marital adjustment, Dual earner couples

INTRODUCTION

Marriage is a lifetime commitment with a person, built upon loyalty, mutual trust, assistance, love, enthusiasm, and understanding. Argument between the needs and demands of the partners forced by the surroundings often direct the problems to adjustment in their relationship.[1] Adjustment in marital life is taken as the method of adaptation between the spouses, which is happened in a gradual way throughout the marital life. Marital adjustment manipulates the numerous features of a person and human society like qualities, work tensions, psychological well-being, sadness, qualification, sexual contentment, manners, pleasure and achievement in the lifetime.[2]

Due to their jobs couples can't pay proper attention to their marital duties and in turn their family life suffers. In societies like Pakistan, family is the basic unit because collectivistic culture system exists here and a disturbed married life will direct to a distress society. Lack of sacrifice, forced marriages, insatiability, combined family system, and distinction in social status seems to be the major reasons for the increased separations.[3] There is an integral need to observe the positive effect of Emotional Intelligence and managing skills up to marital adjustment which will help couple to direct a happy and well-adjusted married life.

Perceived Stress is defined as, 'a process in which environmental hassle exceeds the adaptive capability of an organism, resulting in psychological and biological changes that may place persons at risk for disease'.[4] Stress is a notion that has gained a huge attention in marital studies during the last decade, showing that it plays a significant role in considering the quality and solidity of close relationship. Many studies suggest that constant worry could be a threat to the quality of marital life and its durability. Dual earner couples are highly mutually dependent. So, the perception of stress by the husband or better half not only have an impact on his/her own marital adjustment but also on their partner's matrimonial value.[5]

Emotional Intelligence is an important part of social development and it adds the value to interpersonal relationship.[6] Emotional Intelligence was taken as the capacity to observe, comprehend and control the emotions. The complete intelligence of emotions is importantly associated with happiness of the married couple. Hence, in a marital bond, Emotional Intelligence is exhibited as well as exercised when the two of partners are conscious of their person's emotions and they deal with them in a good way and pay attention to the feelings of their spouse.[7]

Coping is an attempt by a person to solve life stressor and emotional pain.[8] Stress was recognized as maximizing the chances of separation, ultimately producing low association status. Like a tensed spouse may carry his/her stress at the house, that may impact the other partner negatively.[9] Marital adjustment provide an exclusive chance for the investigators to read coping attempts with prospecting a close relationship having arguments and handling them. Skills of coping are often bonded with the concept of adjusting marriage. Dissatisfaction in a wedding is caused by the removal of Coping ways while the contentment in a marriage is due to presence of approach based coping strategies.[10] The aim of this study was to find out the relationship among perceived stress, emotional intelligence, coping strategies and marital adjustment in dual earner couples and explore the gender difference in study variables.

METHODOLOGY

The present research was a cross-sectional with correlation research design and this was approved by Ethical Committee of Riphah Institute of Clinical and Professional Psychology. Non-probability purposive sampling approach was done to enlist the sample. The sample size was calculated through the G-power analysis with 95% confidence interval, 50% error of margin, and 50% response distribution. The participants (n=150) of this study include 75 husbands and 75 wives dual earner couples. The data was collected from different Government and private institutes of Lahore City, Pakistan.

The inclusion criteria of the study were ages of the couples between 25 and 45 years, both partners employed, dual earner couples living together and had passed at least one year of marriage. All those couples who had previous history of divorce and with any serious medical or psychological illness were excluded from the study. The couples having any child with disability were also not included in the study.

The demographic information of participants was obtained through a questionnaire. Perceived Stress Scale[11] (PSS) was used to calculate the level of stressed circumstances in an individual's past month. This scale contains the 14 items rated on a 5-point Likert scale (0=never, 1=Almost Never, 2=Sometimes, 3=Fairly Often, 4=Very Often). The scores of PSS are achieved through the reverse scoring procedure on the items. Items 4, 5, 6, 7, 9, 10, and 13 are the positive stated items. Coefficient alpha reliability for PSS has ranged from 0.84 to point 0.86. Urdu version of PSS[12] was used in the study, with alpha coefficient 0.64.

Schutte Self Report Emotional Intelligence Test[6] (SSEIT) is based on 33 items. Participants respond to each item using a 5-point scale, including 1 as 'strongly disagree', 2 as 'disagree', 3 as 'undecided', 4 as 'agree', and 5 as 'strongly agree'. Total scores are

calculated by reverse coding items 5, 28, and 33 and then summing all items. Scores can range from 33 to 165 with higher scores indicating more characteristic of emotional intelligence. The authors reported two-week test-retest reliability at 0.78 and alpha co-efficient reliability was 0.87. The current study used The Urdu adaptation of this test with reliability coefficient 0.89.[13]

The Brief COPE Inventory[14] (BCOPEI) has 28 statements that evaluate the tendency in which an individual employs various coping techniques. This inventory based on 4-points Likert ranging from 1, 'I haven't been doing this at all' to 4, 'I've been doing this a lot'. Higher score symbolizes the greater extent of coping strategies. This inventory contains the reliability of 0.96. The alpha reliability of Urdu version is 0.82.[15]

Revised Dyadic Adjustment Scale[16] (RDAS) consists of 14 items on which the participants appraise his/her adjustment on a 5-point Likert scale 0.48 are the cut-off score which explained that the score of 48 or above highlighted the highest level of marital adjustment and below score show lowest marital adjustment. The RADS have the excellent degree of reliability which is 0.90. Revised Dyadic Adjustment Scale was translated into Urdu for present study, with alpha coefficient 0.84.

Formal permission was granted from the original authors to use and translate the measures. Permission was also taken from the authors who adapted the PSS, SSEIT and BCOPEI into Urdu. For this study, Revised Dyadic Adjustment Scale was translated into Urdu by follow the MAPI guidelines. The data was collected, after getting the approval from the heads of Government and private institutes of Lahore city of Pakistan. The nature and the purpose of the study was described to the couples and ensured that all the collected information was kept confidential. Written informed consent was taken from the participants. All scales were individually administered to each participant.

Data were entered and analysed on SPSS-21. The Descriptive Statistics were used to enlighten the demographic variables of the research. Pearson's Product Moment Correlation analysis was carried out to observe the relationship among perceived stress, emotional intelligence, coping strategies and marital adjustment in dual earner couples. Multiple regression analysis was done for prediction about these conducted variables among dual earner couples. Independent sample t-test was performed to appraise the gender differences in study variables, and $p \leq 0.05$ was considered statistically significant.

RESULTS

In total 150 cases, there were 75 (50%) husbands and 75 (50%) wives selected with the age range 25–45 years.

Table-1 represents the descriptive statistics of demographic variables of the participants.

Table-1: Frequency and percentage of the demographic variables of the participants (n=150)

Demographics variables	Frequency	Percentage
Education		
Intermediate	12	8.0
Graduate	32	21.3
Masters	87	58.0
M. Phil	15	10.0
PhD	4	2.7
Profession		
Government Jobs	38	25.3
Private Jobs	112	74.4
Job Nature		
Full Time	142	97.4
Part Time	8	5.3
Monthly Income		
20,000–50,000	98	65.3
51,000–80,000	52	34.7
No. of Dependents		
1–5	93	62.0
6–10	57	38.0
Family System		
Nuclear	64	42.7
Joint	86	57.3
Social Status		
Upper Class	33	22.0
Middle Class	117	78.0
Marriage Duration		
1–3	14	9.3
4–6	56	37.3
7–9	60	40.0
10–12	20	13.3
No. of Children		
One Child	39	26.0
Two Children	45	30.5
Three Children	42	28.3
Four Children	16	11.0
Five Children	8	4.2
Psychological Disorder		
No	150	100
Physical Disorder		
No	150	100

Correlations analysis (Table-2) depicted a significant negative correlation between perceived stress and marital adjustment (p=0.001). Perceived stress also had the significant negative relationship with emotional intelligence (p=0.000). Findings also indicated that the emotional intelligence has highly significant positive correlation with coping strategies (p=0.000) and dyadic adjustment (p=0.000). Moreover, coping strategies had significant positive relationship with marital adjustment (p=0.033).

Table-3 shows the multiple regression analysis for the prediction of marital adjustment. The regression model illustrated 21% variance in marital adjustment F (3, 146)=14.348, p=0.000. The results of multiple regression analysis demonstrated that perceived stress (p=0.23) and coping strategies (p=0.92) do not predict marital adjustment but Emotional Intelligence predicts the marital adjustment (p=0.000).

Independent sample t-test is discussed in Table-4 and the results reveal that both the husbands and wives were not significantly different regarding perceived stress (p=0.50), emotional intelligence (p=0.39), coping strategies (p=0.14) and marital adjustment (p=0.03). The effect size (d=0.1) confirmed a trivial effect size for gender with respect to perceived stress, emotional intelligence and marital adjustment. Effect size (d=0.2) in relation to coping strategies illustrated that there is small gender effect size.

Table-2: Correlations between perceived stress, emotional intelligence, coping strategies and marital adjustment

Measures	PSS	SSEIT	BCOP	RDAS
PSS		-0.36**	0.01	-0.25**
SSEIT			0.36**	0.46**
BCOPI				0.15*
RDAS				

*p<0.05, **p<0.01, PSS=Perceived Stress Scale, SSEIT=Schutte Self Report Emotional Intelligence Test, BCOPI=Brief Cop Inventory, RDAS=Revised Dyadic Adjustment Scale

Table-3: Multiple regression analysis where the predictors perceived stress, emotional intelligence, coping strategies and outcome variable that was marital adjustment

Variables	Marital Adjustment		
	B	SE	β
PSS	-0.12	0.10	-0.09
SSEIT	0.26	0.05	0.43*
BCOPI	-0.006	0.06	-0.00

*p<0.01, PSS=Perceived Stress Scale, SSEIT=Schutte Self Report Emotional Intelligence Test, BCOPI=Brief Cop Inventory, RDAS=Revised Dyadic Adjustment Scale, R=0.477, R2=0.22, ΔR2=0.21, SE=Standard Error

Table-4: Gender difference regarding perceived stress, emotional intelligence, coping strategies and marital adjustment (n=150)

Measures	Male (n=75) Mean±SD	Female (n=75) Mean±(SD)	t	Df	p	95% CI		Cohen's d
						LL	UL	
PSS	20.56±7.40	21.34±7.10	-0.66	148	0.50	-3.12	1.55	0.10
SSEIT	130.14±15.53	127.98±15.40	0.85	148	0.39	-2.83	7.15	0.13
BCOPI	69.77±11.22	72.41±11.05	-1.45	148	0.14	-6.23	0.95	0.23
RDAS	55.17±9.80	53.57±9.13	1.03	148	0.30	-1.4	4.65	0.16

CI=confidence interval, LL=lower limit, UL=upper limit, PSS=Perceived Stress Scale, SSEIT=Schutte Self Report Emotional Intelligence Test, BCOPI=Brief Cop Inventory, RDAS=Revised Dyadic Adjustment Scale

DISCUSSION

Findings of the present study depicted that there was a significant negative relationship between perceived stress and marital adjustment. Results also revealed that emotional intelligence and coping strategies have significant positive relationship with marital adjustment. These results are line up with the existing literature. One study that explain the link between perceived stress and adjustment of marriage, suggested that Couples that perceived their lives tensed may add problems to couples' relationship.[17] There was another study based on emotional intelligence and marital adjustment, stated that there was a highly significant positive relationship between emotional intelligence and marital adjustment.[18] Furthermore, a study illustrates the relationship between coping strategies and marital adjustment concluded that, coping skills had a positive connection with the adjustment of marriage of dual earner couples.[19]

The current research also concluded that perceived stress and coping strategies not considered a good predictor for marital adjustment but the emotional intelligence considered a strong predictor of wedding adjustment. It was seen that perceived stress did not forecast the marital quality; this might be due to the fact of cultural differences or Due to having a better understanding the emotions of others, dual earner couples do not let the perceive stress to have an effect on their married life. Furthermore, Empirical evidence confirmed that coping style is not a good predictor of spouse adjustment.[20] Another study investigated the role of Emotional Intelligence in the forecast of marital quality of the dual earner spouses. Consequences of their study explained that Emotional Intelligence was positively considerable in the prediction of marital quality.[21]

The results of Student's *t*-test analysis indicated that husbands and wives were not significantly different regarding the study variables. These results are accordance with the previous literature regarding perceived stress, emotional intelligence, coping strategies and marital adjustment. One study which was regarding to perceive stress concluded that husbands and wives did not behave differently in the perception of stress.[22] Moreover, the research regarding emotional intelligence and marital adjustment, reported that male and female are the same in emotional intelligence and they also enlightened that both gender had equal value on marital adjustment scale.[23] In addition, one study related to coping strategy, explained that husbands and wives are equal in their coping mechanism.[24]

The research has partial generalize ability because of that the data collection was done only from the city of Lahore, Pakistan. So, in future the researcher should select the data from all the cities of a country. A further limitation might be that demographic variables have the greater importance in perceived stress, emotional intelligence, coping strategies and marital adjustment. Consequently, future researchers must consider the demographic variables in studying perceived stress, emotional intelligence, coping strategies and marital adjustment.

CONCLUSION

Perceived stress displayed the negative effect on marital adjustment whereas emotional intelligence and coping strategies have positive impact on marital adjustment of dual earner couples. The husbands and wives were not significantly different regarding the study variables.

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ORIGINAL ARTICLE
HOUSEHOLD CHAOS, MENTAL HEALTH AND SOCIAL ADAPTIVE FUNCTIONING OF ADOLESCENTS

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Background: Management of disturbances becomes hard due to level of chaos that promptly affect the mental health and social adaptive functioning of an adolescent. Mental health plays an important role in the cognitive functioning of an individual. Social adaptive functioning is linked with academic performance and personal working of an individual. The immense and enduring effects of these variables among adolescents may cause the psychological and physical impairment. Objective of this study was to observe the relationship among household chaos, mental health and social adaptive functioning. **Method:** Correlational study method was used to assess the relationship among all the variables. Convenient sampling technique was used to collect the data. Confusion hubbub and order scale, mental health inventory and child and adolescents social adaptive functioning scale were used to measure the study variables. **Results:** Correlational analysis showed significant negative correlation of household with mental health and social adaptive functioning. Regression analysis showed that household chaos significantly predicts mental health and social adaptive functioning of adolescents. Significant differences were also observed between boys and girls in perceived household chaos. **Conclusion:** Adolescents who have high level of chaos at home suffer from mental health issues and lack of social adaptive functions. Findings have implications for parents, health professionals and academicians. Reducing chaos at home can lead to improvement in well being and enhance social adaptive functioning of adolescents.
Keywords: Household Chaos, Mental Health, Social Adaptive Functioning, Adolescents

INTRODUCTION

Household chaos is generally characterized as an arrangement of uncontrolled movement, absence of structure, irregularity in normal routine and elevated level of surrounding stimulation.[1] Chaotic home situations generally related with an unfriendly environment result in the development of child which continue in youth and adulthood. Household chaos is usually associated with the factors like academic achievement, behavioural issues, socioeconomic condition, cognitive abilities, and emotional functioning.[2] In early adolescence, individuals suffer from poverty, socioemotional issues, helplessness, distress and critical cognitive development.[3] Evans recognized the household chaos as crowded, loud, confused, poor settings for child development.[4,5] Mental health includes our social, emotional and psychological wellbeing. It influences how we think, feel, and act. Mental health and wellbeing is always characterized to be without any mental disorder. Studies have explored that adolescents are more sensitive towards the traumatic events and health issues. The intensity of adolescents' response towards the stressful events depends on their mental health and the skills they adopt. Wellbeing is a key aspect of mental health which is characterized in terms of good or bad.[6] The term adaptive functioning illustrates the self-sufficient character of an individual for the real life situations.[7] It describes the skills such as social, academic, communication, and daily living skills. Social functioning is a set of self-sufficient behaviour of a person that is comprised of social skills, social behaviour and social cognitions.[8] Household chaos is a risk factor for executive functioning and influences the adaptive functioning of adolescents.[9] Individuals with chaotic home environments exhibit low academic achievement and less adaptive behavior.[10] Chaos in a home environment provides a poor condition for learning for a student.[11] Household chaos affects psychological wellbeing.[12] The theory of chaos explains that psychological wellbeing gets affected by the harmful risk factors of chaos in adolescents.[13] On the other hand, psychological distress shows a significant positive correlation with household chaos.

Chaos is a factor that leads to lower wellbeing and causes more distress. Chaos at home disturbs the social adapting function of an individual. Poor performance of children at school is related to the disturbances at home.[14] Homes that are disordered, render chaotic environment and do not offer a conducive environment for learning through regularities, schedules, organized and rich surroundings always restrict the healthy development of adolescent.[15,16] The World Health Organization (WHO) defines adolescent age as between 10 and 19 years. The period of puberty is divided into three periods which are the start 10–13 years, middle 14–17 years, and 18–21 years for late adults.[17] Adolescent is a very sensitive

period in which mostly individuals are under psychological, emotional, and social pressures. It was hypothesized that chaos has significant negative correlation with mental health and social adaptive functioning of adolescents. Another hypothesis formulated on the basis of assumption that gender may differ with regards to study variables. The present work attempts to study the relationship between household chaos, mental health and social adaptive functioning among adolescents.

METHODOLOGY

It was a cross-sectional study conducted at National university of Modern Languages, Islamabad from March to August 2020 after approval from Board of Advanced Studies and Research. Convenience sampling technique was used to collect the data. Sample of the study consisted of 200 adolescents aged 10 to 19 years. Inclusion criteria was adolescent in above mentioned age group and being a student, as one scale CASAFS was used specifically for students.

Participants were 81 males and 119 females. Sample was taken from Rawalpindi/Islamabad, Sargodha and Faisalabad. Participants recruited in the study belonged to different socioeconomic status. Urdu translated version of all instruments was used. To measure the household chaos, Confusion, Hubbub and Order Scale (CHAOS) with 15 items was used. This scale has acceptable alpha reliability of 0.79, and 0.83, and predictive validity[18,19]. To assess the level of social adaptive functioning, Child and Adolescent Social Adaptive Functioning Scale (CASAFS) that consisted of 28 items was used. This instrument shows adequate levels of internal consistency ranging from 0.67 to 0.81.

Mental Health Inventory (MHI) with 38 items was used to measure the psychological wellbeing and psychological distress. For Mental Health Scale, the estimates of internal consistency were high[20], alpha reliability being 0.95.

After taking formal permission from parents and teachers, and with the consent of participants, questionnaires were handed over to them. Data was collected in person by providing the questionnaires to the participants along with a demographic sheet and consent form in Urdu.

RESULTS

Results indicate the descriptive statistics, psychometric properties with alpha coefficients of reliability and Pearson's correlation coefficient among all the study variables. Table-1 shows demographic details of the variables. Out of 200 participants 81 (40.5%) were boys and 119 (59.5%) were girls. The average age of participants was 16.6 ± 2.32 years.

Table-2 depicts the correlation among all the variables which is negative but significant ($p < 0.05$). Psychometric properties show the alpha reliability of all the variables ranges between 0.72 to 0.75 (Table-3).

Student's t-test revealed that significant differences were observed in ender groups between all study variables (Table-4)

Table-1: Demographic characteristics (n=200)

Variables	Frequency	Percentage
Age		
10–14 Years	55	27.5
15–19 Years	145	72.5
Gender		
Boys	81	40.5
Girls	119	59.5
Socio Economic Status		
Lower class	74	37.0
Middle class	89	44.5
Upper class	37	18.5

Table-2: Psychometric properties and correlation coefficient between CHAOS, MHI and CASAFS

Scales	CHAOS	MHI	CASAFS
CHAOS	-	-0.158*	-0.341**
MHI	-	-	0.103
CASAFS	-	-	-
Alpha	0.75	0.72	0.74
Mean	11.12	137.9	8.96
SD	3.54	15.29	8.69
Skewness	1.28	-0.255	-0.268
Kurtosis	-0.401	6.76	1.04

*$p < 0.05$, **$p < 0.01$

Table-3: Linear regression analysis predicting mental health and social adaptive functioning with chaos

Variables	Mental health			Social adaptive functioning		
	B	SE B	β	B	SE B	β
Household chaos	145.5	3.53	-0.158*	77.4	1.93	-0.314**
R^2	0.20			0.90		
F for change in R^2	5.09			21.6		

*$p < 0.05$, **$p < 0.01$

Table-4: Gender-wise differences in household chaos, mental health and social adaptive functioning (n=200)

Scales	Boys (n=81) Mean±SD	Girls (n=119) Mean±SD	t	p	95% Cl LL	UL	Cohen's d
CHAOS	10.02±2.71	11.86±3.85	-3.71	0.001	-2.81	-0.864	0.552
MHI	142.7±15.0	134.6±14.6	3.83	0.928	3.97	12.3	0.551
CASAFS	70.49±8.62	67.84±8.62	2.13	0.460	0.195	5.09	0.307

DISCUSSION

The aim of this study was to find out the relationship between study variables and to investigate the effect of household chaos on mental health and social adaptive functioning. There was significant negative correlation of household chaos with mental health and social adaptive functioning. Previous findings also highlighted that household chaos has negative relationship with mental health.[21] Earlier findings on chaos at home and its relationship with cognitive ability and socioemotional

adjustment of school children indicated that home chaos had an impact on behavioural problems, study skills and on adjustment factor. The children with chaotic home environment had low academic achievement.[22] A recent study also demonstrated the negative effect of household chaos on child executive functioning.[23] These findings indicate that high level of household chaos is related to lower level of mental health and poor social adaptive functioning. Regression analysis showed that 20% of variance in mental health and 90% of variance in social adaptive functioning was explained by household chaos. Gender-wise difference revealed significant differences in perceived household chaos. Mean scores indicated that girls perceived higher level of home chaos. No significant gender-wise difference was found in mental health and social adaptive functioning of adolescents.

The present study provides awareness regarding household effects on mental health and social adaptive functioning of adolescents. It gives insight about the factors of chaos at home which disturb the mental health (psychological wellbeing and psychological distress) and social adaptive functioning (school performance, peer relationship, family relationship and home duties/self-care).

CONCLUSION

Chaos at home affects the mental health and social adaptive functioning of adolescents. Efforts should be made to control the level of chaos at home to improve the wellbeing and academic achievement of adolescents.

LIMITATIONS

This study was conducted with a small sample of 200 from only three cities. The present study relied on self-report measures; future studies may use behavioural indices to measure chaos and social adaptive functioning to enhance the authenticity of findings.

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REVIEW ARTICLE

TRAUMATIC BRAIN INJURY ASSESSMENT USING GLASGOW COMA SCALE: A LITERATURE REVIEW

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Objective: The objective of this study was to analyse the Glasgow Coma Scale (GCS) reporting and recognize causes for inaccuracy of GCS implications. **Literature selection and critical appraisal:** Literature search was carried out by using specific keywords on PubMed, Google Scholar, and Science Direct. The GCS definitions, present status of GCS reporting, frequency and time of assessment, assessment schemes and confounders were critically analysed. **Results:** More than 90% of the publications using GCS scoring cite the 14-item GCS rather than the 15-item GCS. The timing of the initial GCS assessment is inconstant. GCS components are seldom utilized, contributing to the loss of information. Confounders are often not reported and, if they are, not in a standardized manner. The order of the GCS components is not consistent. **Conclusion:** The current inconsistent and inappropriate use of GCS diminishes its reliability in both clinical and scientific context. A consensus statement is needed to correct this situation. Citing the correct references, early and repeated GCS assessments at defined intervals, standardized reporting of confounders and GCS component and scores. Utilization of a uniform assessment scheme is recommended.
Keywords: Neurological evaluations, Glasgow Coma Scale, Coma, Brain injury, Accident, Trauma

INTRODUCTION

The Glasgow Coma Scale (GCS) score has become the standard criterion to assess the neurological status of brain-injured patients. The GCS was developed in 1974 as an effort to assess different groups of patients with altered levels of consciousness[1], and to improve communication between healthcare personnel caring for patients with impaired consciousness. After modification, a new GCS based on a 15-point numeric score was adopted for the assessment of traumatic brain injury (TBI).[2]

The three components (eye-opening, verbal and motor response) of the GCS assess the function of the cerebral cortex and the upper brainstem, the reticular activating system. The eye-opening response measures the arousal mechanism of the brainstem; the verbal response, the integration of cerebral cortex and brainstem; and the motor response, the integrity of cerebral cortex and spinal cord.[3]

The GCS has some limitations. For example, brainstem reflexes and eye movements are not considered. The GCS is, however, an important instrument for decision making, which is used in combination with other diagnostics such as CT scan and pupillary reaction. These evaluations can indicate the need for referral to a tertiary hospital with on-site neurosurgical facilities like CT scanning after brain injury or surgery.[2]

The purpose of this review was to describe the current state of inter-rater reliability and accuracy of GCS scoring and to identify reasons for any shortcomings. In addition, this study proposes strategies

for more consistent and accurate scoring, hopefully initiating a consensus process for improved GCS scoring.

SELECTION OF LITERATURE

By using specific keywords on PubMed, Google Scholar, and ISI web, literature was searched for period of publication from 2012 to 2021. Two comprehensive searches were conducted. Firstly, the term GCS and Glasgow Coma Scale were distinctly combined as acronym with agreement, inter-rater, accuracy, precision and performance. Secondly, GCS and Glasgow Coma Scale were combined with instrument, education, and training. For further articles there were no language-related restrictions in searches.

All types of research methods like randomized control trials, registered case studies, cohort studies, databases, case series, case studies, and abstracts were included for search. Letters and comments were excluded for the study. Present situation of GCS reporting, its time, definitions, confounders and frequency of assessment, assessment plans, and scoring were critically analysed.

MAJOR FINDINGS FROM LITERATURE

Latest picture of GSC scoring

Many studies were conducted in early 1990s, focused on diverse professional cohorts and diversity of approaches, but GCS were not documented in pre-hospital setting. Lack of 56% of cases of pre-hospital GCS assessment in traumatic brain injury patients was noted. This lack of performance based on experience of healthcare professionals. Highly experienced

professionals showed greater inter-rater consistency as show in Table-1. This inter-rater consistency was not absolute even in trained physicians. A recent study conducted in Emergency Department showed only 32% of cases were assessed by well-trained physicians.[4]

One study investigating inter-rater reliability and accuracy of GCS in nurses working in different acute medical settings was based on videotaped patients.[5] Among non-physicians and physicians, inter-rater reliability was observed, however same limitations were observed between nurses and physicians (Table-2). Only one-third of these nurses correctly rated the motor component of the GCS, about one-half the eye-opening component, and >80% correctly rated the verbal component. Nurses with more neurosurgical experience and a higher educational qualification

rated more accurately.[5] Similar results were observed as among physicians or among nurses (Table-3, 4).

In one-third of cases, assessment is inappropriate scoring of GCS. Accuracy and inter-rater reliability differ according to variety of healthcare professionals and their experience. Differences were observed between the same specialties, and also in inter- and intra-canter GCS assessment. In patients with unchanged state of consciousness and high variability, GCS scoring will be misleading low, and this will be misleading healthcare professionals for needless referrals, CT-scans and surgical interventions. It is astonishing that in last 25 years, there were insufficient initiatives for quality improvement of GCS scoring accuracy.[6,7] Contributing factors to inappropriate GSC scoring are stated below (Table-5, 6).

Table-1: Comparison studies of (EMS-GCS) pre-hospital GCS assessment, and (ED-GCS) hospital GCS assessment

Sample size	Study setting	Types of patients	Pre-hospital HCP	Hospital HCP	Major research findings	Research limitations	Reference
n= 12882	ED, field	Major injury	Paramedics	ED staff	Strongly correlated	Some registered data was missing	8
n= 3052	ED, field	Injury	Paramedics	ED staff	GCS agreement: moderate-high	Time difference > 20 mints	9
n=7823	Not defined	Injury	Paramedics	ED physician	Very strong relationship	Short description of GCS categories	10
n= 33	Field, ED,	TBI	Paramedics	ED staff	No correlation	Small sample size	11
n= 60	ED, Field	TBI	Pre-hospital physician	Senior physician	2 points under estimation of (EMS-GCS)	Time gap 32 mints	12

*n: Number of Patients, HCP: Health Care Provider

Table-2: GCS performance comparison between inexperienced and experienced healthcare provider

Research Setting	Type of patients	Inexperienced HCP	Experienced HCP	Major findings	Limitations	Reference
ED	Neurological	Nurses with <2 years' experience	Experienced Nurses	Incompetent eye assessment in GCS among inexperienced nurses	No regularity of verbal stimulus	13
Computer lab	Trauma	4th Professional medical students	Senior physician	Correct response was moderate (>75%)	14 points tool	14
Neurosurgical wards	Multiple trauma	4th Professional medical students	Senior physician	Correct response was mild (<50%)	Various countries setting	15
Trauma Centres	Traumatic brain injury	Nursing students	Registered nurses	Mild accuracy among nursing students	Small sample size	16
	Traumatic brain injury	Medical assistants	Physicians	Variability was greater among inexperienced HCP	Small sample size	17

ED: Emergency Department, TBI: Traumatic Brain Injury, HCP: Healthcare Provider

Table-3: Studies regarding GCS performance comparison between physicians

Research Setting	Type of patients	Physician 1	Physician 2	Major findings	Limitations	Reference
ED	Neurological	Residents	Emergency physicians	Inter-rater compatibility was moderate	Small sample size	18
Paediatric ED	Blunt TBI	Emergency physicians	Emergency physicians	Inter-rater compatibility was Good	Most of GCS was high	13
ED	Medical Neuro	Emergency physicians	Emergency physicians	Inter-rater compatibility was moderate	None for field exposure	19
ED	ND	Community physicians	Neuro Surgeon	63% similarity in GCS Assessment	Small sample	20
ED	Surgical trauma	Emergency physicians	Emergency physicians	Inter-rater compatibility was good	GCS was high as 15 in 41%	21
Neuro Wards	Vascular and tumour disorders	Neuro surgeon	Neuro surgeon	Inter-rater compatibility was low	Small sample	22
Neuro ICU	Brain haemorrhage	ICU physicians	ICU physicians	Inter-rater compatibility was moderate	Assessment interval was long	17

ED: emergency department, ND: not defined, ICU: intensive care unit

Table-4: Studies regarding GCS performance comparison between nurses

Research Setting	Type of Patients	Nurse 1	Nurse 2	Major Findings	Limitations	Reference
Videotapes, class room	Trauma	CCU, ICU, PACU, ED, NICU Nurses	Experienced nurses	Congruence and accuracy was moderate	No Field Work	14
Emergency Unit	Poisoned	Emergency nurses	Emergency nurses	Inter-rater congruence was Good	Sample size was small	15
Intensive Care Unit	Unconscious, intubated	Intensive care Unit Nurses	Intensive care unit nurses	Inter-rater congruence was good	Sample size was small	20

PACU: post-anesthesia care unit, CCU: coronary care unit, GCS: Glasgow Coma Scale, NICU: neonatal intensive care unit, ICU: intensive care unit. ED: emergency department

GCS sub-scoring

Mattei and Teasdale[1] initially recommended presenting the sub-score information by means of a profile, but in subsequent publications the use of a sum score was proposed.[23] Accordingly, many studies that include patients with TBI report only the GCS sum score. Providing only the total score results is a significant loss of information and may diminish predictive validity.

Different Definitions of the GCS

A 14-item GCS tool consisting of three components: best verbal response (5 points) the best motor response (5 levels) and best eye-opening response (4 points), appeared in 1974.[1] Two years later, articles with 15 points GCS scale were published.[2] One point increased in the best motor response as kind of flexion was categorized into two categories of abnormal flexion and withdrawal. Later in 30 years, mostly researchers adopted the 15-points GCS, however several most referenced articles were not succeeded to even referring the 14-point GCS[24], which mislead researchers as inaccurate GCS scoring in clinical practices and clinical research and educational programs.

GCS assessment time and frequency

The GSC scoring was recognized for in-hospital practice for untreated patients in intensive care emergency units, and neurosurgical wards (Post resuscitation GCS).[7] Later on, when modern emergency medical services were established, GCS performed as pre-hospital assessment[25] exposed no association in pre-hospital and hospital GCS evaluation. There was no analytical value of pre-hospital GCS about the outcome. It was recommended that GCS was efficiently associated with hospital admission.

More than 9,000 moderate to severe non-intubated traumatic brain injury patients had correlation coefficient of 0.67. The mean GCS was 11.4 on scene and 11.5 on hospital admission. There was difference between emergency department and pre-hospital GCS assessment findings in patients with different transport timings. It also reported by Leitgeb et al[6], but in contrast no change over time was observed by another study[17]. In Europe where

physicians' practice outside the hospital is common, GCS is less common in hospital assessments, often based on inappropriate analysis of data.

Confounding Factors

Managing traumatic brain injury patients with anaesthesia, neuromuscular blockers, and endotracheal intubation makes GCS evaluation a challenge. There are different methods for assessing the oral and ocular opening of the GCS in patients who are intubated and/or sedated. GCS scoring is valid in neuromuscular blockers, irreversible tetraplegia and polyneuropathy. In some hospitals, medical professionals rate each eye open and 1 point for oral response to narcotics and intubated patients. Some defer the rate of the eye-opening component until the anaesthesia and analgesia subside, although they rate the noise response by a score of 1.[26]

There are other factors that affect GCS accuracy in traumatic brain injury. The GCS can predict brain injury in 13% of patients with traumatic brain injury. GCS scoring is low and inaccurate in narcotic and intubated patients.[26] Pharmacologically induced coma also lowers GCS scoring ratings and many research studies ignore to discuss these confounders.

GCS Assessment Planning

Currently, there are two GCS schemes in use each with different sequences of the three components. One sequence is listed as best eye opening, best motor, and best verbal responses (E-M-V sequence); and the other, as best eye-opening, best verbal and best motor responses (E-V-M sequence). Studies that do not mention the sequence of tested GCS components tend to use the E-V-M sequence. This sequence may be preferable as it follows the sequence of a systematic clinical investigation of the patient as well as the increasing number of the maximal sub-score (E: 4, V: 5, and M: 6), making memorization and application easier.

Implication for Practice

Literature suggests the best use of GCS scoring (E4, V5, M6). Correct referencing is important for accurate use of an instrument, otherwise biases and uncertainty may be introduced.[18]

Table-5: Comparison studies about GCS scoring between physician and non-physician

Research Setting	Type of patients	Physicians	Non-physicians	Major findings	Limitations	Reference
Emergency Unit	Neurological	Emergency physicians	Emergency nurse	Inter-rater congruence was low	Self-selection bias, most with high GCS	27
Emergency Unit	Neurological	Not defined	Emergency medical technician	Inter-rater congruence was good	Fluctuations of GCS assessment time	28
Videotapes	Not defined	Emergency physicians	Paramedical staff	2 points GCS under assessment by paramedics	Sample size	29
Emergency Department and community setting	Trauma patients	Emergency physicians	Paramedical staff	Inter-rater congruence was excellent	No field experience	15
Videotapes	Neurological patients	Intensive Care physicians	ICU and emergency nurses	Inter-rater congruence was moderate	No field experience	26
Films	Not defined	Neurosurgeons	Neuro surgical and medical nurses	Inter-rater congruence was moderate	Only motor response, 14-point scale	17

Table-6: Studies about major trials regarding use of GCS among brain trauma patients

Study content	Research design	Study setting	Assessment sequence	GCS scoring	GCS definition	References
Data Bank about traumatic coma	Prospective Cohort	Emergency and intensive care units	Eye, verbal, motor	Sum score	Not defined	17
TBI and emergency services	Prospective Cohort	Emergency ward	Motor	Components score (As Eye, Verbal, Motor)	6 points	11
TBI risk factors and seizures in TBI	Prospective Cohort	Not defined	Eye, verbal, motor	Sum score	15 points	13
Rules for CT scan	Randomized Control Trial	Field	Not defined	Sum score	15 points	1
TBI and hypothermia	Randomized Control Trial	Emergency unit	Not defined	Sum score	15 points	9
TBI and hypertonic saline	Randomized Control Trial	Emergency unit	Not defined	Sum score	15 points	16
TBI and corticosteroids	Randomized Control Trial	Emergency unit	Eye, verbal, motor	Sum Score	Not Defined	3

Initial and Subsequent GCS Reassessment

Out-of-hospital emergency medical services are key players in the assessment of consciousness. They have the opportunity to assess the patient at an early stage before beginning resuscitation. Therefore, in the pre-hospital setting this study proposes to assess the GCS upon initiating the ABCDE resuscitation, but before endotracheal intubation. To obtain the most reliable information, GCS assessment should be performed repeatedly within the first 24 hours and include data from the prehospital setting. All assessments should be reported. This proposition is based on the observation that GCS scores of up to 30% of all TBI patients deteriorated or improved secondarily when compared to initial values.[20]

Accurate documentation of the time point of GCS assessments including the approximate time of injury or the documented time could be highly relevant for the estimation of brain injury severity and for research purposes.[16]

Confounder identification

GCS scoring is evidently affected by many confounding reasons like sedation, alcohol, and endotracheal intubation (Table-7).

Table-7: Confounders that affect GCS scoring

Injury
Multiple injuries
Periorbital swelling in facial trauma
Eye injury
Spinal injury
Hypoxia in thoracic injury
Hypotension in shock
Neuromuscular diseases
Medical disorders
Cerebral diseases
Sedatives
Medicines
Mechanical devices

Component reporting

As others[14], this study proposes to report the GCS components in addition to the sum score. This component reporting may avoid loss of information, and improve accuracy as verified with GCS of 4. The E1, V2, M1 had a mortality rate of 28%, while the mortality rate was twice high (52%) with E1, V1, M2 combination.

Uniform Scheme utilization

The same GCS scheme is easy to communicate and memorize. This study highlight the components of GCS

in the pattern of best eye openings, positive verbal, and motor responses (4-5-6) that sequence demonstrates sound clinical trials.

1. Talk patiently (Open eyes)
2. Try to respond quickly with words
3. Assess for motor response

An identical plan also improved the accuracy and inters-rater reliability as proven by 4th year students from Switzerland, Basel University.[27]

Consensus Statement Call

Many distracting factors are associated to inaccurate, variables and absent characterizations are involved in GCS assessment. Hence an agreement supported by international experts and based on best evidence are required. Following situations should require for GCS assessment:

1. During a primary examination prior to difficult interventions
2. For sedated and intubated patients

Leads for Quality Improvement Plans

The local quality improvement plan will be mandatory for the effective use of the GCS as it proves that GCS scores and confusing test training are important. A study emphasized that complicated programmes are capable, if provision of Pre- and Post-GCS assessment training Programme is added.[19] For GCS assessment, written checklist must be part of these training sessions. Practical skills for GCS assessment for exercise on real life simulation scenarios for knowledge enhancement for patient management and treatment as well as computer-based training tools are also useful.[18]

Research for Level of Consciousness Assessment

Elements made easier to report only part of the motor assessment that may increase road reliability and accuracy reduced each analysis as evidenced by Alhassan *et al*[14], an increase inter-rater reliability between 83%, compared to 71% of motor assessment and 42% of GCS through motor component. However, these results are less reliable because they have been tested in undiagnosed trauma patients, not in traumatic brain patients.

The independent variables that were related to the GCS scores were pupillary reaction, CT visibility and age. Opening of the eyes and oral constituents were also very essential. The most appropriate analysts were the period for prothrombin, glucose, platelets, haemoglobin, hypoxia, and hypotension. GCS during hospitalization and other forecasts play an important role in long-term outcomes. It is important to inspect the GCS motor component from pre-hospital admission to within 24 hours after injury.

A new scale for coma having four points was recently introduced in the emergency departments and in Intensive Care Units.[20] These four points have four elements (visual response, motor response, mental thinking, and breathing) but they do not have an oral response, they are important for intubated patients. Recent studies have proven that four points are better for decision making compared to GCS motor component. With long-term results, the motor component of GCS segment with student responses has shown strong analysists.

CONCLUSION

All possible factors of inaccuracy in assessment of GCS scoring are acknowledged in researches and clinical practice because each one of these possible factors can be modified. GCS scoring improved performance and enhanced the quality of GCS by using standardized approach. For correction of this situation by applying early and repeated GCS assessment in defined intervals, accurate reference, standardized reporting, GCS components and scores, and constant assessment schemes are suggested. A recognized board agreement articulation ought to stimulate quality advancement programs for more accurate and dependable GCS scoring.

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